A SIMULATION OF HUMAN NERVOUS AND CARDIOVASCULAR SYSTEMS

By

P. C. PANDEY

DEPARTMENT OF ELECTRICAL ENGINEERING

INDIAN INSTITUTE OF TECHNOLOGY KANPUR

SEPTEMBER, 1981

A SIMULATION OF HUMAN NERVOUS AND CARDIOVASCULAR SYSTEMS

A Thesis Submitted
in Partial Fulfilment of the Requirements
for the Degree of

MASTER OF TECHNOLOGY

By

P. C. PANDEY

to the

DEPARTMENT OF ELECTRICAL ENGINEERING

INDIAN INSTITUTE OF TECHNOLOGY KANPUR

SEPTEMBER, 1981

माँ की स्मृति को

CERTIFICATE

This is to certify that the work on A SIMULATION OF HUMAN NERVOUS AND CARDIOVASCULAR SYSTEMS has been carried out by Mr. P.C. Pandey under my supervision and this has not been submitted elsewhere for a degree.

R Biswas

Dr. R.N. Biswas 10.8.87.
Professor
Department of Electrical Engineering
Indian Institute of Technology
Kanpur

ACKNOWLEDGEMENTS

Working under the guidance of Dr R N Biswas has been a great experience to me and I wish to acknowledge my deep sense of gratitude to him for his indespensible advices and critical appraisal. I am grateful to Dr K E Hole and Dr S S Prabhu for taking interest in the project.

I am thankful to all the staff members of the department, who directly or indirectly helped and assisted during the work. My special thanks are due to Mr S N Sikdar and Mr S S Bhatnagar for extending all the help and cooperation and Mr V S Yadav and Mr S K Kole (P C Lab) for their enthusiastic efforts in setting up the process for printing the front panel.

I express my thanks to Mr Kamal Kumar and Mr Prem Malhotra for the immense help provided by them in 'burning' the EPROMs. I am grateful to friends - Mr Vinod P Deshmukh, Mr S Ravindhran and Mr Kamal Nayan for help and cooperation throughout the work, Mr Anand V Chaturvedi for the proof reading of the typed manuscript and Mr Jyoti B Bhattacharjee (Bhatta) for the encouragement during the moments of distress. Finally, I wish to express my thanks to all the friends whose company helped in keeping spirits high and stay at IIT-Kanpur pleasant.

The patient, neat and skillful typing of Mrs Kamla Devi is appreciated.

Sept. 2, 1981 (Ganesh Chaturthi)

Prem C Pandey

ABSTRACT

This project is an effort towards modelling and developing an electrical simulation of various activities associated with the nervous and cardiovascular systems.

The neural cell model has been simulated by a circuit incorporating its various analog and digital properties,whil disregarding the shape of action potential waveform. On the other hand, a simulation of the membrane patch with its passive and active properties and an approximation of action potential waveform has been developed.

Using the neural cell model as a basic module, peripheral nervous system and a spinal reflex have been simulated. Higher activities of the central nervous system have been simulated on a microprocessor-based system, incorporating six sensory and four effector channels. By changing a part of software, different kinds of conditioned reflexes,learning processes and vegetative activities can be simulated.

A simplified simulation of blood circulation system alongwith the electrical and pumping activities of the heart has been done. In addition to, automatic mechanism of the heart itself, vegetative control by the central nervous syste also has been simulated. Effects of bleeding, transfusion, physical activity and disorders in the conduction of excitati can be studied on it. Through software, effect of external stimuli on cardiac activities can also be incorporated.

TABLE OF CONTENTS

LIST OF FIGURES

CHAPTER I

INTRODUCTION

The problem of the relation between animate and inanimate matter has excited the interest of mankind since ancient times. Investigations in this direction have proceeded along two lines. The first of these aims at the artificial creation of living matter. Despite the efforts in this direction throughout the history of mankind, the aim has not yet been achieved. The efforts in the second line have attempted to simulate various functions of living organisms by means of inanimate systems. Studies and investigations associated with developing the engineering models simulating the structure or behaviour or [redacted] both of living organisms fulfil several objectives. They help in learning and understanding biological problems. The understanding developed in the process of developing such analogs may lead one to design various kinds of engineering devices utilising to a greater or lesser extent, the principles of the structure of living organisms.

1.1 Modelling Techniques

In developing analogs, both the mathematical and physical modelling methods have been used. Mathematical models have great utility in limited domains. They are

invaluable in cases where the number of variables is reasonably limited and nonlinearities do not present severe analytic difficulties. They are of vital importance, when statistical or probabilistic aspects are decisive such as in the membrane biophysics or the neural network formulations.

Physical models are relatively more tangible than their mathematical counterparts. Depending on how they are made, they may be placed in one of following catagories

(i) Ionic models

(ii) Pneumatic and electro-mechanical model

(iii) Electronic models

(iv) Computer simulated models

1.1.1 Ionic models

These are based on the effects associated with electro-chemical reactions. The most important application of this approach has been in modelling the processes in a nerve cell. However, this approach does not find an extensive use, because the measurements may turn out to be as difficult as in the real situation and further the physical mechanisms may turn out to be as obscure as the real phenomena.

1.1.2 Pneumatic and electromechanical models

The most extensive use of such models has been in simulating blood circulation system and physical movements.

They have been also used for simulating some features of the cell such as adaptational aspects. However because of their cumbersome nature, they are less common.

1.1.3 Electronic analogs

These can simulate continuous variable nonlinear operations economically and quite often accurately. They permit a rapid and effective kind of observer-model interaction as the different time-dependent phenomena can be directly observed while stimuli and model parameters are changed. However, electronic models are not good solution for simulating learning and other brain processes envolving complex neural networks, because the observation and manipulation of parameters become very difficult.

1.1.4 Computer simulated models

Any computer simulated model is essentially an extension of some mathematical model since a set of mathematical equations describing the given phenomena is generally the starting point for this kind of modelling. In this approach, either the analog or the digital or both kind of computers are used. Analog computers permit the direct observation of phenomena, but usually the models based on them tend to be cumbersome as a large no.of modules are needed. The digital processing intrinsically does not permit economical

representation of continuous variable nonlinear interactions. However, the special problems that arise in large network simulation are more readily handled by digital computers than by other techniques. Due to the growing speed and storage capabilities, they may ultimately provide the most satisfactory means for modelling complex neural systems.

1.2 Scope of the present work

Most challenging problem in the area of simulation of structure and behaviour of living organisms has been the one associated with man himself. As the human body involves a tremendously complex set of processes, in any attempt towards simulating one has to limit the scope of the work. In the present work, an effort has been made in the direction of simulating some very simple processes related with the nervous system activities. As an example of various processes in the body that are controlled by the nervous system, as well as have their own automation mechanism, the cardiovascular system has been chosen.

In the second chapter, the properties and features of nerve cell - the basis of entire nervous system are presented. In third chapter, models simulating nerve cell have been proposed. In the next two chapter, the organisation and function of the nervous and cardiovascular systems are discussed. After

presenting a picture of these systems and developing nerve cell models, the simulations developed for the cardiovascular and nervous systems are described in the sixth and seventh chapters respectively. A discription of the overall system is presented in the chapter eight. This concluding chapter suggests the experiments and investigations that can be carried out using the system developed in the project.

CHAPTER II

NERVE AND MUSCLE CELLS

A cell is a basic unit of life capable of independent manifestations of life. In living organisms, it is possible to find cells widely differing from one another. This is the result of the process of evolution necessiating specialisation of individual cells. Aggregates of cells that perform a common physiological function are called tissues. These can be divided into four classes :

(a) Various kinds of epithelia - They form the basis of glandular control.

(b) Muscular tissues - They consist of elongated cells that are capable of contraction when excited by stimuli and thus convert chemical energy directly into mechanical energy. The action of muscular tissue is mostly controlled by the nervous system.

(c) Connective tissues - They bind together the other kind of tissues.

(d) Nervous tissues - They form the basis of nervous control.

Despite the considerable differentiation of all cells, there exist certain properties common to all. However, the nerve and muscle cells have special property that a temporary change in trans-membrane potential (called action potential) is developed upon application of excitation.

2.1 Nerve Cells

A nerve cell (also called neuron) is the fundamental element of the nervous system. Individual nerve cells may differ from one another in anatomical configurations and in functional properties. However, all neurons, regardless of individual differences in shape, size and location have four functional components :

(a) one or more input elements

(b) an integrative element

(c) an active transmission line

(d) one or more output elements

The integrative element is soma or the cell body. There are nerve processes that grow out of the cell body proper and may have a large variety of shapes. The cell body is similar in structure to the cells of other tissues and its diameter varies from several microns to several tens of microns. The processes are small in diameter while their length may run to anything from a fraction of a millimetre to the order of a metre. The inputs to a neuron may occur at several points on its surface. The majority of the inputs, however, enter through short, highly branched processes, called dendrites, which at their terminal ends interface with extensions from other neurons or sensory cells. A long process of approximately uniform diameter is called on axon, which acts

as the active transmission line. The end of the axon is branched to form terminal arborization.

The integrative process either takes place in the dendrites or in the soma. If the sum of input excitations exceeds a threshold level, the cell fires, generating a signal which is actively transmitted down the axon length to the terminal regions. The transmission properties of the axon are bidirectional. However, the nerve cells are connected to one another by means of special nerve endings, called synapses. They incorporate an electrochemical mechanism for information flow from one cell to other cell in one direction only.

The nerve cell like every cell in a living organism contains a fluid, called the intracellular fluid (or the cell plasm), which is separated from the interstitial fluid surrounding and bathing the cell by an extremely thin (50-100 A.U.) membrane. Both of the fluids are ionic solutions, the predominant ions in the interstitial fluid being Na^+ and Cl^-, while the intracellular fluid consists essentially of K^+ ions and an organic ion generally referred to as A^-. The electrochemical processes which give rise to most of the properties of the nerve cells are controlled principally by the permeability of the membrane to these ions. In the so called myelinated axons, the membrane is covered

by a much thicker (2-3 μ) lipo-protein sheath, thereby rendering the membrane impermeable to these ions. The myelin sheath is broken at regular intervals (0.4-2 mm) for about 1μ, thus allowing the migration of ions across the membrane only at these regions, called the nodes of Ranvier.

2.2 Action Potential

The membranes of nerves and some other cells posses the highly distinctive property of being excitable. A potential difference exists across the membrane. This is called membrane potential. In the steady state, the cell remains polarised with the intracellular fluid at a negative potential of 60-100 mV with respect to the interstitial fluid. This potential is called the resting potential. Complex, but shortlived, electrochemical processes propogated on the membrane surface are initiated under the influence of particular stimuli. The electrical response during these processes is called action potential[1,2].

An environmental change brings about a transient depolarisation, usually by increasing the permeability to Na^+ ions. Influx of Na^+ depolarises the membrane, thereby in turn increasing the permeability to Na^+ which leads to further depolarisation. If the original stimulus is capable of depolarising the membrane beyond a threshold value, the process is regenerative. Not only the membrane gets fully depolarised

but even its sign changes (going about 30-70 mv). This rise of impulse constitutes the first phase of action potential. The stimulus serves merely to trigger the cell into activity and an additional increase in stimulus intensity beyond threshold has no effect on the amplitude of action potential. For this reason, it is said to have all-or-none behavior. Towards the end of first phase, the depolarisation peak is followed by a fall in sodium permeability and a rise in potassium permeability. This starts repolarisation process. The accompanied voltage change results in a decrease in Na^+ permeability and after a delay in K^+ permeability also. When repolarisation is complete, K^+ permeability is still above resting value and consequently, the membrane hyperpolarises, going even more negative than the transmembrane potential.

After the end of impulse proper, in the third phase, slower processes related to the membrane returning to the initial state occur. Fig. 2.1 depicts a typical action potential waveform and associated processes.

In a short interval of time after the onset of action potential, the membrane is non-excitable. This interval is called the absolute refractory period. It specifies the maximum impulse repetition rate, usually of the order of 1000 impulses per second.

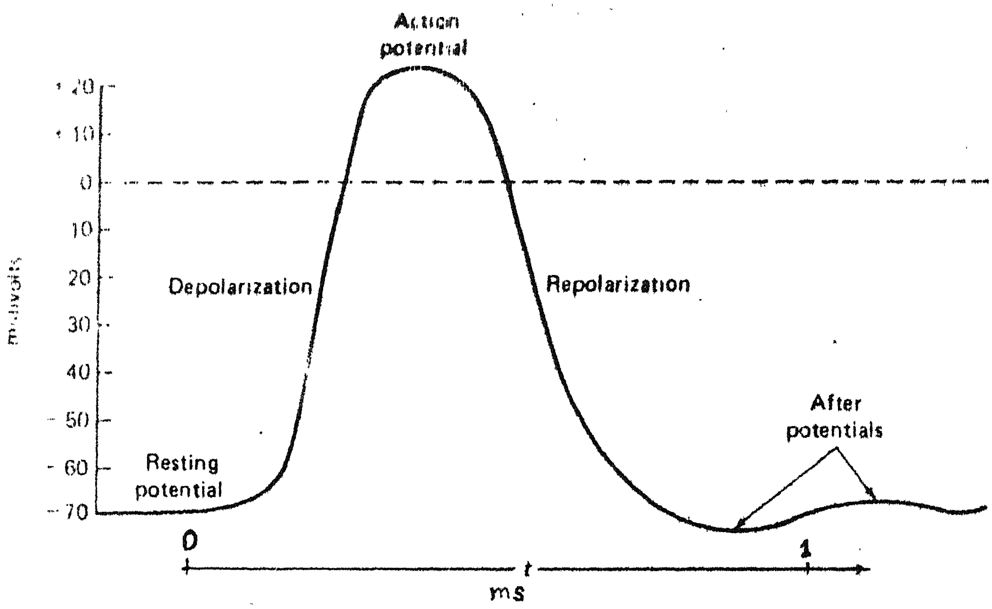


Fig. 2.1 Waveform of the action potential (Time scale varies with the type of cell)

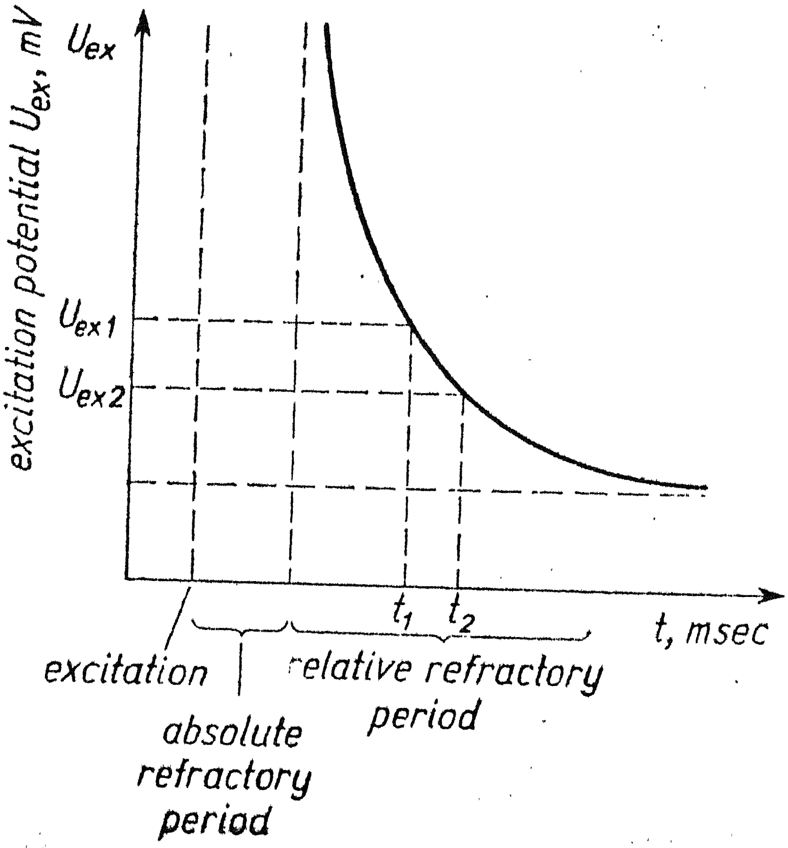


Fig. 2.2 A Simplified diagram of the changes in cell sensitivity after excitation.
U_{ex} - excitatory potential, t - time.

After an absolute refractory period, it is possible but difficult to generate an action potential. This is called the relative refractory period. However, in time the threshold diminishes to the normal value. A typical simplified picture of cell sensitivity after an excitation is given in Fig. 2.2[3].

The plot of changes of excitability as a function of time implies that the higher the excitation potential (Uex) applied to the cell, the shorter the time between individual action potentials. It thus follows that the nerve cell is an element capable of frequency modulation. Shorter interval between pulses and associated higher impulse rates correspond to more intense stimulation.

If the excitation stimulus be applied in the form of a pulse, the strength required to initiate an impulse depends on the duration of the excitation pulse, the relationship is given as :

$$I_{st} = I_{rh} \left(1 - e^{-T/\tau}\right)^{-1} \qquad (2.1)$$

where I_{st} = stimulus strength

T = stimulus pulse width

τ = a parameter characteristic of the membrane passive properties

I_{rh} = stimulus strength to initiate an impulse when $T \to \infty$. This is known as rheobasic stimulus.

2.3 Nerve Conduction

For subthreshold stimulation, the propagation along the axon length is analogous to that in a passive electric cable and is referred to as electrotonic conduction. The velocity and attenuation are decided by its passive properties such as resistances of the intracellular and interstitial fluids, dielectric constant and leakage conductance of membrane etc.

The important mode of propagation as regards the transmission of information is the suprathreshold propagation. As the stimulus exceeds the threshold, an action potential is developed. The process involves a short section of the membrane. However, the sudden change in the transmembrane potential during the first phase leads to the flow of surface currents and thus results in a rise in transmembrane potential at neighbouring points of the cell membrane. When this change exceeds threshold, action potentials are generated. As the action potential propagates along the active membrane, it leaves the points through which it has passed in refractory period and they will not respond to the surface currents due to neighbouring regions. Propagation of action potential thus takes place only in the direction of the incident wave.

In unmyelinated fibres, the stimuli propagate relatively slowly (about 1 metre per second or so). Myelination greatly increases the conduction speed and thus decreases the reaction

time in the nervous system. The action potential is generated only at the nodes of Ranvier, the propagation being electrotonic in the myelin-sheathed segments. As this region has far less capacitance and leakage conductance compared to an unmyelinated fibre of same length and diameter, the speed of conduction is much higher. Owing to the attenuation associated with electrotonic propagation, the amplitude of the impulse is considerably reduced when it reaches the next node, but is still large enough to excite it. Thus the depolarization jumps from one node to the other and this mode of conduction is referred to as saltatory conduction or step conduction.

2.4 Synaptic Conduction

The conduction between mutually interactive nerve cells is through a synapse. A single axon may form synaptic connections to many nerve cells. The axonal side of the synapse is referred to as presynaptic region, the corresponding portion of the succeeding cell is termed as post-synaptic. The separation between pre-and post-synaptic membranes, called synaptic gap is of the order of 200 A.U.

Under the influence of impulses arriving at the presynaptic knob, a special activiting substance called mediator is released from the vesicles at the membrane. This secretion induces a rise in sodium permeability of post synaptic membrane resulting in an increase in transmembrane potential.

This is referred to as excitatory postsynaptic potential (EPSP). At some junctions, an inhibitory mediator is released, causing hyperpolarisation of the membrane. This is called inhibitory postsynaptic potential (IPSP).

The synaptic space also contains a substance causing decomposition of the mediator. Due to its action membrane potential returns to its original value. However if the postsynaptic potential exceeds the threshold, regenerative depolarisation starts and action potential is generated. The process of excitation or inhibition of the synapse delays the transmission of signals from one neuron to the other. This delay, called synaptic delay, is of the order of 0.5 msec. The axonal delay, which depends on the speed of propagation and the length of the axon is in the range of 0.1 - 20 msec.

A nerve cell is induced by stimuli from many synapses on the cell body and dendrites alike. This is called spatial summation. Further, since the mediator secreted by the synapse decomposes with a certain time constant (2-4 msec), impulses which arrived at the synapse earlier also have some contribution in the formation of net excitatory potential. This phenomenon is called temporal summation.

2.5 Muscle Cells

The electrical properties of voluntary or skeletal muscle cells are comparable to those of nonmyelinated axons.

Differences between muscles and nerves lie mainly in the special anatomical features of muscle cell and in the role played by Ca^{++} ions in muscle excitation [4]. An action potential initiated at one end of a muscle fibre spreads by virtue of local current effects to the other end. The action potential is accompanied by a contraction.

A skeletal muscle is built-up from a set of individual 10-100 μ-thick fibres which are functionally separable. Increasing the stimulus strength to a muscle produces an increasing response until a maximum level is reached. The increasing response results from an increase in the number of activated fibres. When a stimulus initiats a propagated action potential on a fibre, resulting contraction throughout the fibre is maximum. When a stimulus does not initiate propagation, the contraction is confined to activated region alone.

Efferent (or motor) nerve fibres convey electrical activity to the appropriate muscle leading to its contraction. Each axon normally activates from 3 to 150 muscle fibres. The interface between a motor nerve ending and a muscle fibre is known as the neuromuscular junction. The mechanism involved is similar to the one in synapse. The neuromuscular delay ranges from 0.5 to 1.5 msec.

2.6 Receptors

Physical stimuli like light, heat, pressure, odour etc are converted into neural signals by a set of specialised cells known as receptors. Stimulation of a receptor cell produces a decrease in membrane polarisation, called the generator or receptor potential. Its value is related to the intensity of the stimulus and is graded as well as stationary. Each receptor is primarily responsive to a particular form of energy; thus there are optoreceptors, presso-receptors, chemoreceptors etc. Some receptors respond only to unidirectional change while some are primarily responsive to the rate of change in the stimulus intensity.

If a steady state stimulus is applied, the resulting generator potential will ordinarily diminish with time. This decrease in potential is called adaptation. For some kind of receptors a decrease from the initial value to a lower steady state value is observed.[5,6,7]

CHAPTER III

NERVE CELL SIMULATION

A nerve cell is an analog digital element, and is thus distinguished from the fundamental components used in data processing and automatic control systems. The following is a list of well established properties of the nerve cell[1] -

i) A cell may have a number of excitatory as well as inhibitory input channels and only one output channel, viz - axon.

ii) The input channels (through synapses or dendrites) incorporate spatial and temporal summation.

iii) The output of a nerve cell follows the " all or none " principle.

iv) An impulse or a series of impulses is generated when the net excitation exceeds a certain threshold.

v) Postsynaptic changes in excitability (absolute and relative refractory periods) are associated with the generation of each impulse and as a consequence of these changes, the firing frequency is modulated by the value of suprathreshold excitation.

vi) An impulse is generated by a cell with some delay (so-called synaptic delay) after the arrival of suprathreshold stimulus. The extent of this delay depends on the intensity of the stimulus and on the state of membrane excitability at the given moment.

Some other properties attributed to nerve cells include - variations in the weights (effectiveness in inducing the impulse) of synaptical inputs and arbitrary adaptational changes in the threshold.

Most neuron models can be classified in two primary catagories - (i) those modelling patches of the excitable membrane and (ii) those representing input-output relationships for the whole neuron.

3.1 Membrane Patch Models

The earliest physical model of excitable membrane and axon is the ionic model using "iron-nitric acid" system.[2] Most modern models are however, electronic in nature. One branch of electronic models is centred around the development of 'neuristors' based on a concept introduced by Crane.[3] The major emphasis in this kind of studies[3-6] has been on a device having the form of a one dimensional channel along which signals may flow, the signals taking the form of propagating discharges having the following properties -

(i) threshold stimulatibility

(ii) uniform velocity of propagation

(iii) lossless propagation

(iv) refractory period following a discharge

Most of the other models are based on the mathematical model for a neural membrane given by Hodgkin-Huxley.[7] Many complex models[8-11] have been devised, which do incorporate subthreshold passive responses as well as action potential generation, often to the point of identifying the transmembrane ionic currents involved.

Most of these models are relatively complex and are thus uneconomic for extensive neural networks.

A relatively 'simple model incorporating both active and passive properties may be constructed' based on the conventional representation of an axon, as shown in fig. 3.1. It breaks the axon into discrete segments and represents the axoplasmic resistance by Ra, the extracellular resistance by Re, the transmembrane leakage resistance by R_m transmembrane capacitance by C_m and the active process involved in the generation of the action potential by a nonlinear time varying resistance R_{HH}. Brockman[12] has proposed a simple two-transister circuit simulating R_m, C_m and R_{HH}.

3.1.1 Brockman's membrane model

The basic circuit as proposed by Brockman is shown in fig. 3.2, which is essentially a collector coupled controlled astable with a large base resistance R_2 at Q_1. To explain the operation of the circuit, let us first consider the

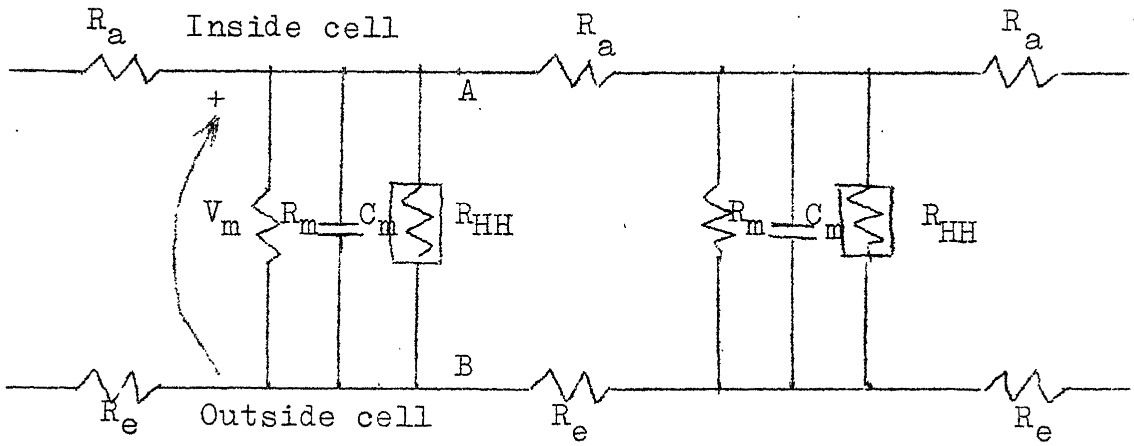
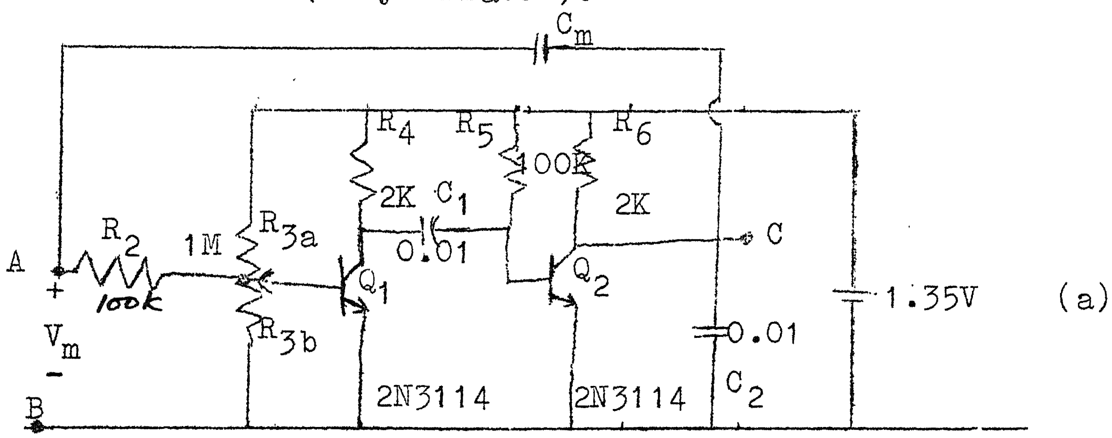


Fig. 3.1 Equivalent representation for a axon (unmyelinated).



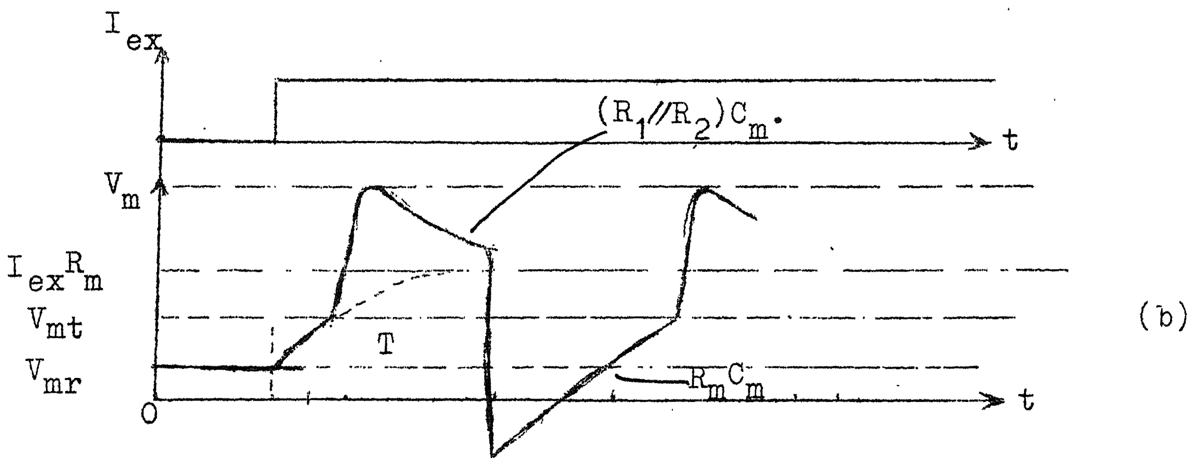


Fig. 3.2 (a) Brockman's model

(b) Response to a step excitation.

condition for d-c steady state to exist and then R_3 establishes bias such that Q_1 is in cutoff while R_5 biases Q_2 in saturation. The impedance looking into terminals A-B is then a capacitance C_m (in series with the small saturation resistance of Q_2) in parallel with a resistance R_m given by

$$R_m = R_1 \parallel (R_2 + (R_{3a} \parallel R_{3b})) \tag{3.1}$$

As long as the transmembrane voltage V_m does not rise to a voltage where Q_1 begins to conduct, the membrane is adequately represented by these passive elements.

Let us consider the effect of a gradual increase in V_m. As V_m increases the threshold V_T ; given by the equation

$$V_T = [R_2 + (R_{3a} \parallel R_{3b})] \; V_\gamma/(R_{3a} \parallel R_{3b})$$

$$- [(R_2 \parallel R_{3b})V_{cc} \; (R_2+(R_{3a} \parallel R_{3b}))]/[(R_{3a}+(R_2 \parallel R_{3b}))(R_{3a} \parallel R_{3b})] \tag{3.2}$$

Q_1 begins to conduct and because of the loop gain being more than one, a regenerative action takes place. The rise in voltage at point A corresponds to the first phase of an action potential (depolarisation of the membrane). The duration of the pulse at A is determined by $R_5 \; C_1$. The fall in the voltage corresponds to the repolarisation phase. By a proper choice of

C_1 and C_m ratio, the hyperpolarisation phase also can be observed in the form of V_m undershooting below the resting value.

If the model is excited by a current I_{ex}, V_m starts rising towards I_{ex}. R_m with a time constant R_m C_m. In case I_{ex} $R_m > V_T$, there is a firing the moment V_m exceeds V_T. Following the pulse, the process of charging C_m starts again and a volley of impulses result.

Brockman studied the behaviour of an axon simulated by connecting sections of this membrane patch model with R_A= 10K and R_E = 0 (allowing the use of a single power source) and has reported that the phenomena of electrotonic and action potential propagation are reasonably simulated by this model.

This model can be used for simulating myelinated as well as unmyelinated fibres. In the case of myelinated fibres,this active network is placed at the points corresponding to the nodes of Ranvier,connected by passive R-C ladders.

This circuit exhibits relative refractory period and thus is capable of frequency modulation. However, it does not exhibit an absolute refractory period. The impulse waveform is not a good approximation of the action potential and the threshold is not accurately adjustable. Further, the amount

of undershoot at the end of the impulse depends on the pulse width (determined by R_5 C_1) and hence the refractory period and pulse width cannot be varied independently.

3.1.2 A modified membrane patch model (version - I)

The simple model proposed by Brockman may be modified to incorporate an absolute refractory period, which can be achieved by inhibiting the input for certain period immediately after the end of the pulse. This has been done by including a transister Q_3 (as shown in fig.3.3) in the model. Because of its base circuitry, Q_3 is off under d.c steady state. At the rising end of pulse, diode D conducts for a short time, quickly discharging capacitance C_3 as V_{c1} falls. The rise is rounded because of the effect of C_2. At the end of pulse, the regenerative process is somewhat slowed down because of effects of C_2 and C_3, but if R_4 C_3 , R_6 $C_2 << R_m$ C_m , it will still result in a termination of the pulse with an undershoot which is arrested to $- 2V_D$ and quickly comes back. The rise in V_{CE1} turns Q_3 on which prohibits excitation as the stimulating current is shunted by its collector. It comes out of this state after a time, corresponding to absolute refractory period, which is determined by $(R_7 + R_4)C_3$.

In addition to the incorporation of an absolute refractory period, the circuit has the additional advantage

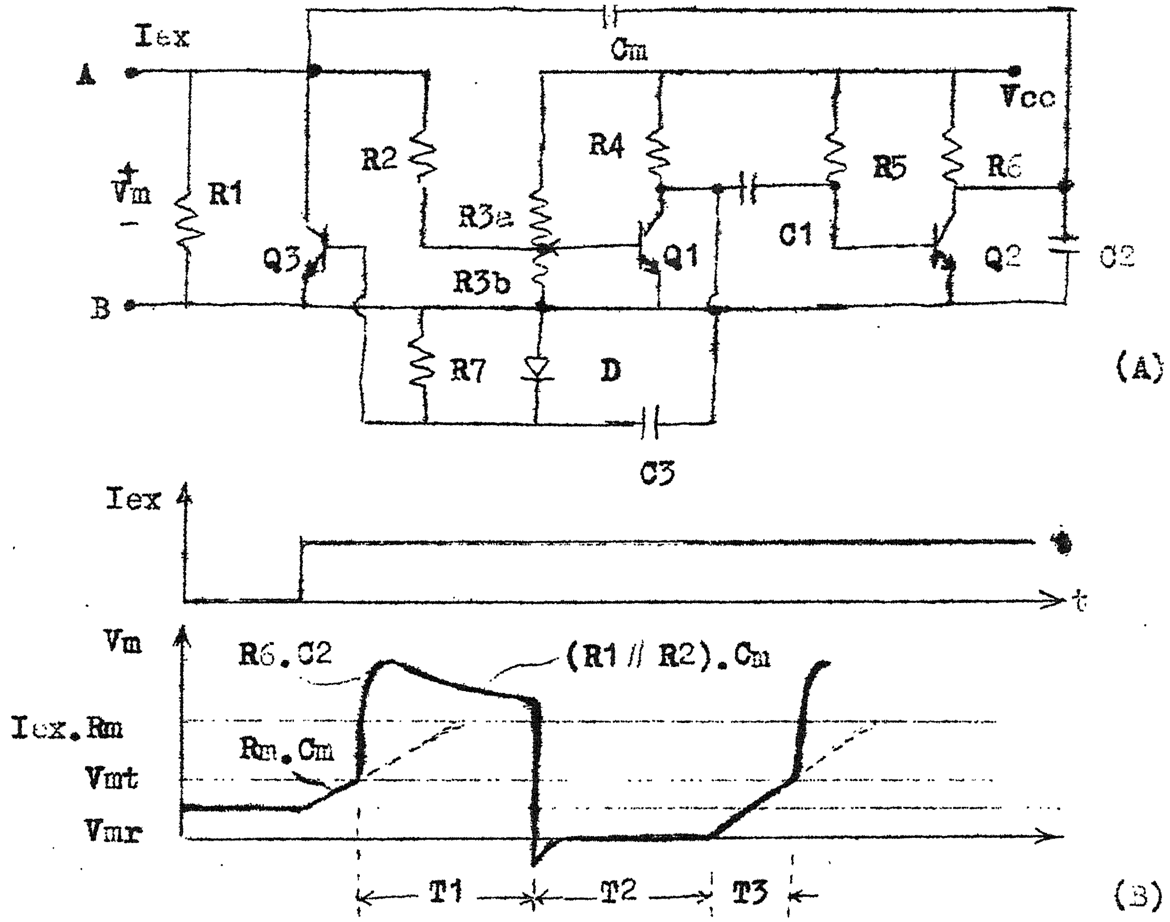


Fig. 3.3 Modified membrane patch model (I)

(A) Circuit , (B) Response to step excitation

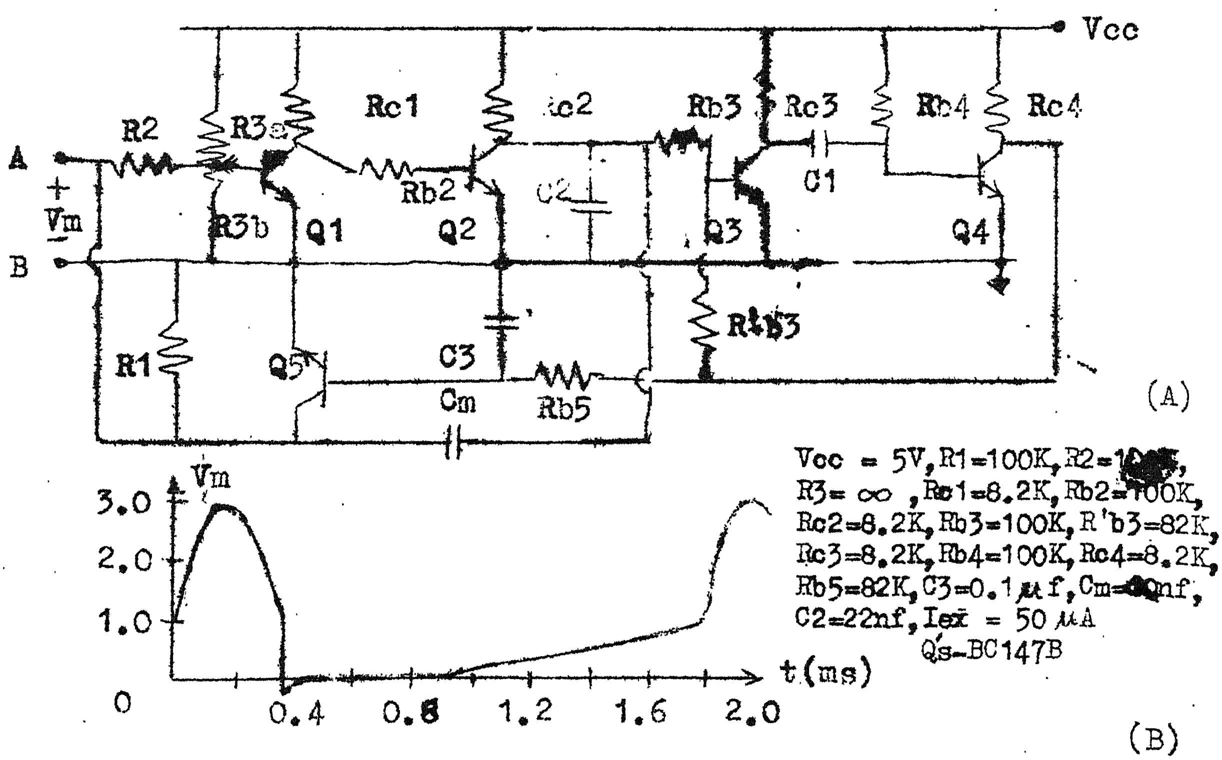


Fig. 3.4 Modified membrane patch model (II)

(A) Circuit, (B) Waveform of Vm for subrathreshold excitation

that at the end of absolute refractory period, v_m is at V_{CES}; irrespective of ratio of C_m and C_1 and thus the pulse width and relative refractory period may be varied independently.

3.1.3 Modified membrane patch model (version II)

The modified version discussed earlier does incorporate an absolute refractory period, but the waveform of the impulse is not a good approximation of action potential. An approximation of action potential waveform may be achieved by using separate sections in the circuit, controlling the various phases of the impulse activity. A realisation of such a circuit, while still retaining the basic properties of earlier model has been developed as shown in fig. 3.4. In the d.c steady state Q_1, Q_3 and Q_5 are off and Q_2 and Q_4 are on. Thus for subthreshold signals, the properties are the same as discussed for earlier two models. Q_1-Q_2 and Q_3-Q_4 form two monostables. As v_m exceeds the threshold due to a suprathreshold current excitation, the first monostable triggers and voltage at A goes high. As the rise in V_{c2} (slowed by R_{c2} C_2)reaches a threshold the second monostable triggers, which after a delay (due to effect of C_3) turns Q_5 on and thus process of depolarisation starts. Q_5 remains on for the second monostable pulse duration thus providing an absolute refractory period (determined by R_{B4} C_1).

Except for the later portion of falling edge, the impulse -waveform is a good approximation of action potential. The falling edge may be made more smooth by introducing an R-C ladder at the base of Q_5. This circuit also suffers from the lack of an accurate adjustment of threshold.

3.2 Neural Cell Models

When one is primarily interested in the function of a nerve cell in information processing, rather than in the mechanisms underlying this function, many of the complexities related to active processes and shape of waveform of action potential may be ignored while modelling.

Most of the models[13] simulating the input-output relationship for the whole neuron rather than small areas of membrane separate the input terminal from the point where modelled transmembrane voltage is developed. The earlier efforts in this kind of modelling were making use of discrete components. The basic problems associated with these models are the complexity of the circuit and a large number of undetermined parameters. In the more recent models[14,15,16] integrated circuits have been used. However, the no.of chips (typically 3 to 10) and the interactive nature of parameters are the basic hurdles in using them for extensive neural studies.

The emphasis in the present work has been in constructing a simple model with a reasonable functional representation. For the purpose of simulation, the various processes associated with neural activity have been divided in three sections, and a circuit simulating each has been developed (fig.3.5). The first circuit has many inputs and simulates the properties of temporal and spatial summation as well as adaptation. Its output is graded and hence is termed as generator potential corresponding to a receptor cell output and the effect of synapses. The second circuit is the action potential generation block which converts the graded generator potential into a volley of impulses. The third circuit is an active delay line simulating the lossless propagation along the axon length.

3.2.1 Generator Potential Block

For the simulation of various analog processes viz - adaptation, temporal and spatial summation, circuit shown in fig. 3.6 has been developed. Circuit in fig. 3.6a simulates the effects due to an excitatory input channel. Combination of R_1, R_2 and C_1 simulates the process of adaptation. The process of temporal summation (integration) is simulated by the combination of R_3, R_4, C_3. The build-up time constant corresponding to the release of the chemical transmitter at

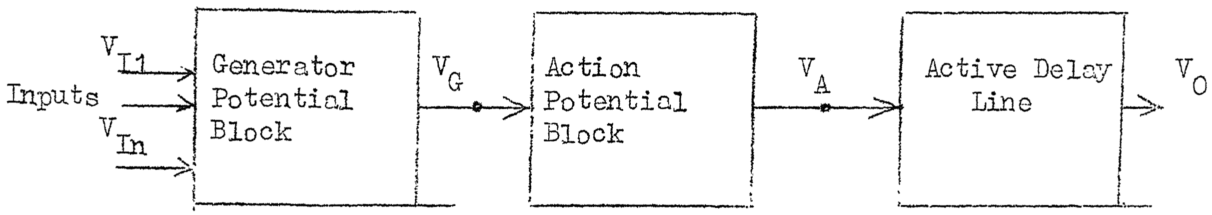


Fig. 3.5. Nerve cell, represented as three blocks

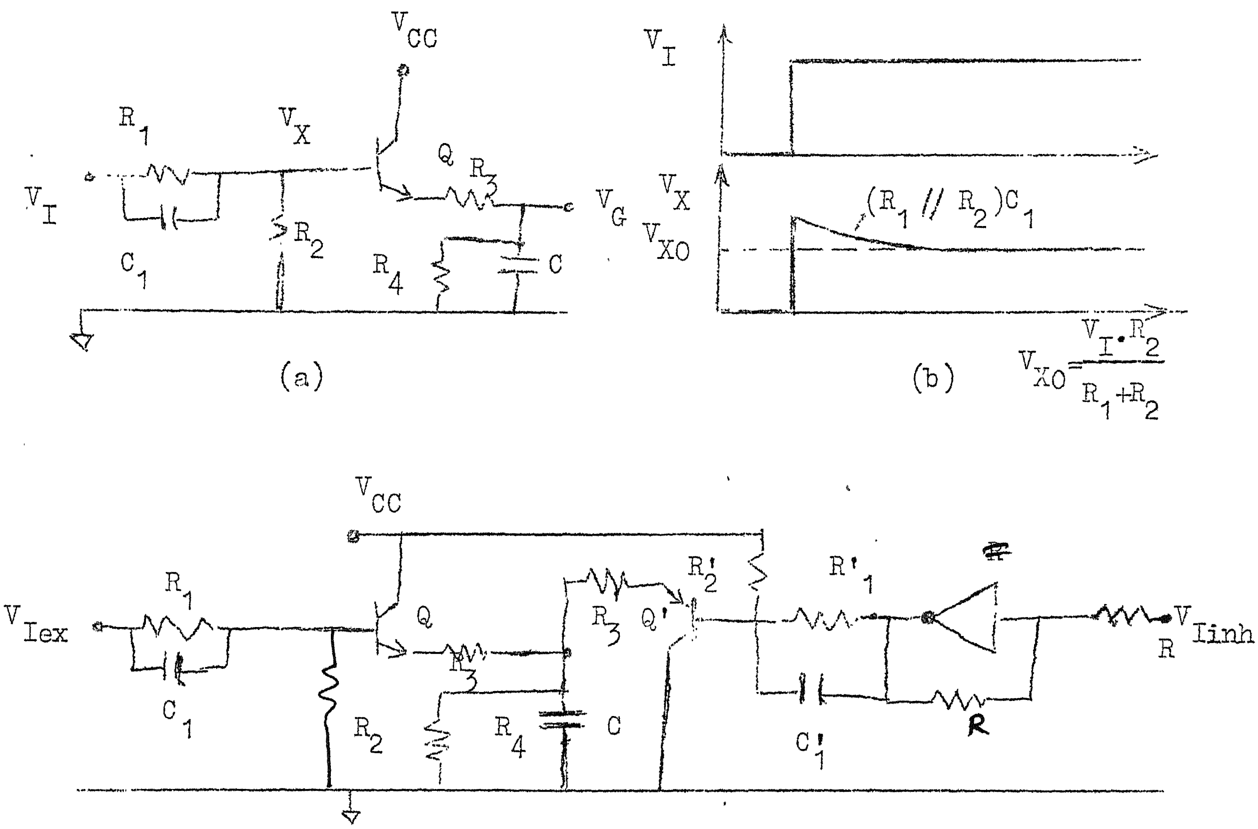


Fig. 3.6 Generator Potential Block
(a) Circuit showing one excitating input
(b) Effect of adaptation
(c) Circuit showing one excitating and one inhibitory input.

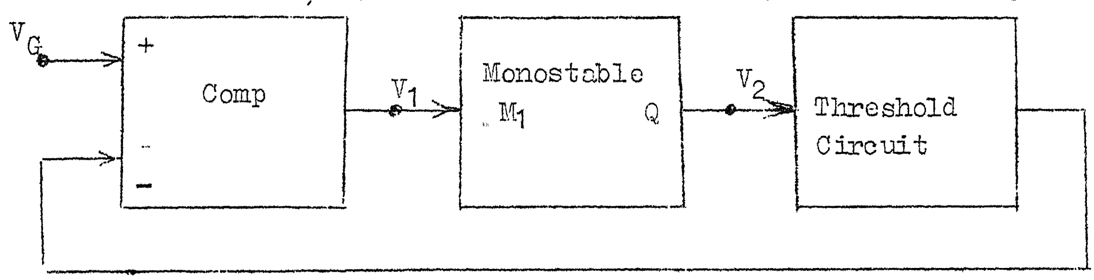


Fig. 3.7 Scheme for action potential generator block.

the synapse is controlled by R_3 C_3 while the decay time constant, corresponding to the decomposition of chemical transmitter in the synaptic gap is controlled by R_4 C_3. Fig. 3.6c includes the effect due to an inhibitory input channel also. The components and the time constants are in correspondence with the ones for excitatory inputs. A number of excitatory and inhibitory inputs may be connected together with C_3 as the capacitor on which temporal and spatial summation of charges take place. The transistors interfacing the adaptation and summation may be looked upon as synapses with unidirectional transmission property.

3.2.2 Action potential block

Action potential generation can be simulated by a simple scheme shown in fig. 3.7. The input voltage V_G (generator potential, the output of the first circuit) is continuously compared with a threshold V_T. When V_G exceeds V_T, comparator output V_1 goes high and pulse is generated at the monostable output. Falling edge of pulse triggers the threshold circuit and its output goes high ; and hence comparator output goes low. The threshold remains at high level for a certain duration corresponding to absolute refractory period and then starts decaying towards its steady state value with certain time constant. Another pulse is generated as soon as V_T has fallen

below V_G. This process results in an encoding of the magnitude in the form of frequency of pulses.

The threshold circuit may be realised by a negative edge triggered monostable determining the absolute refractory period with a circuit giving a decaying threshold after this period as shown in fig. 3.8. Steady state threshold is determined by R_x and R_y while decay rate is controlled by $C\ (R_x // R_y)$.

This scheme may be realised in a number of ways using commercially available monostable and comparator ICs. However, it is possible to use timers in place of the monostables as the inputs to them remain in steady state for the duration of quasi-stable state. As the time-durations involved are of the order of a ms, CMOS inverting gates have been used. The comparator also may be made with four CMOS inverting gates [Appendix]. Thus the whole scheme has been realised with one CMOS chip with six inverting gates and one PNP transistor as shown in fig. 3.9.

Steady state threshold V_{Tr} is given as

$$V_{Tr} \simeq (R_3 / R_3 + R_4)\ V_{cc} \qquad (3.3)$$

(neglecting the effect due to R_B)

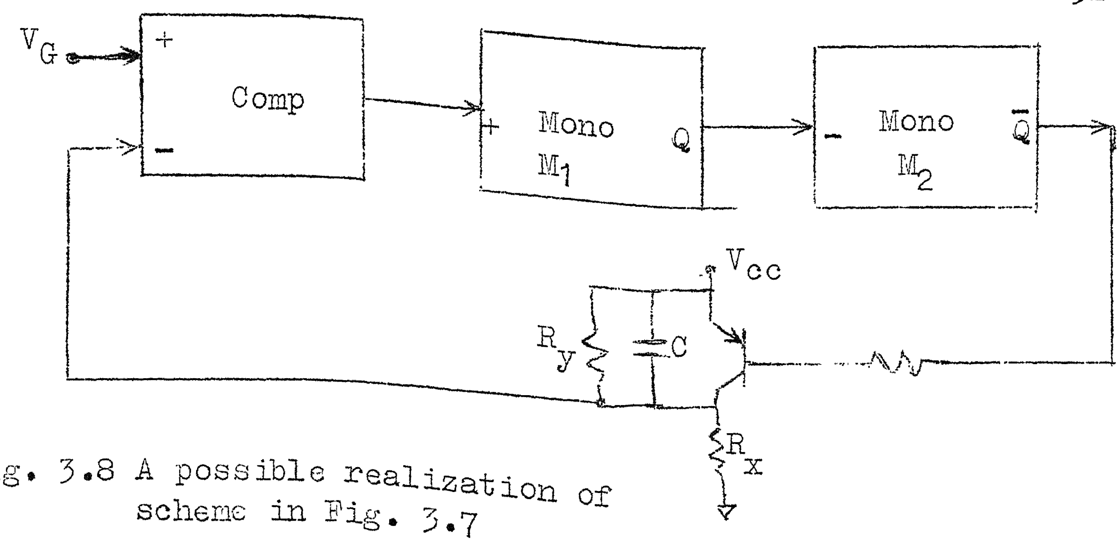
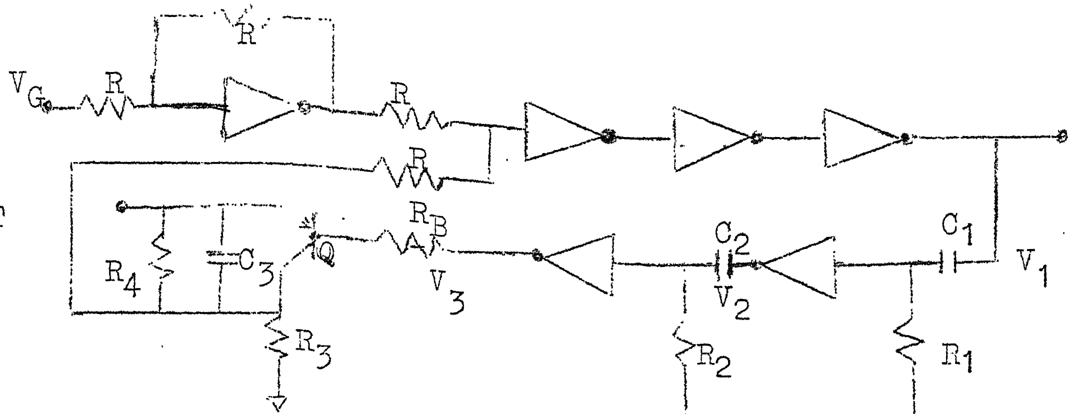


Fig. 3.8 A possible realization of scheme in Fig. 3.7



(a)

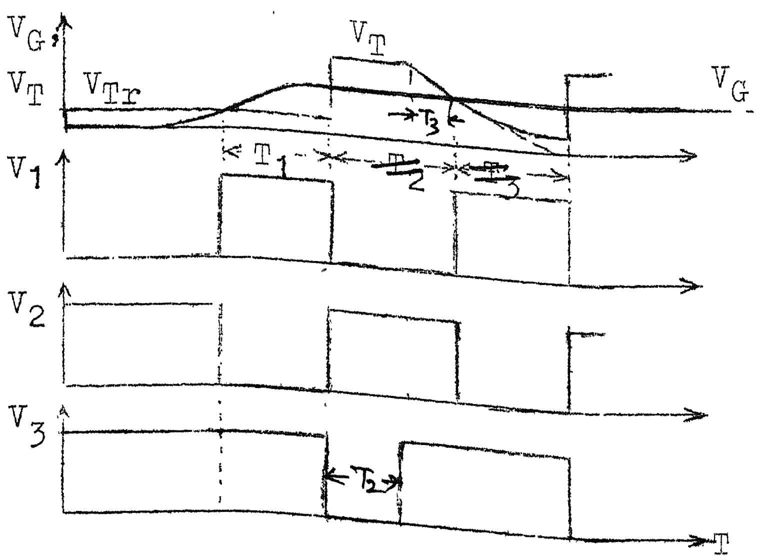


Fig. 3.1 Action potential generator using CMOS inverting gates

(a) Circuit (b) Waveforms

Pulse widths of the two timers, T_1 and T_2 are given as

$$T_1 = R_1 C_1 \, l_n \, (V_{OH} / V_t) \simeq 0.7 \, R_1 C_1 \qquad (3.4)$$

$$T_2 = R_2 C_2 \, l_n \, (V_{OH} / V_t) \simeq 0.7 \, R_2 C_2 \qquad (3.5)$$

where V_t = threshold of the CMOS gate.

For the absolute refractory period, the threshold remains at $V_{cc} - V_{CES}$ as Q is driven to saturation. To ensure that Q goes to saturation during this period,

$$R_B \gtrsim \beta \, R_3 \qquad (3.6)$$

where β = dc current gain of Q.

Following the absolute refractory period, V_2 goes high ; and hence Q cuts off. V_T decays to its steady state value with a time constant τ.

$$\tau \simeq (R_3 \quad R_4) \, C_3 \qquad (3.7)$$

Threshold voltage is given as

$$V_T = ((V_{CC} - V_{CES}) - V_{Tr}) \, e^{-t/\tau} + V_{Tr} \qquad (3.8)$$

Another pulse is generated after a time T_3, when V_T just falls below V_G. Thus we have

$$T_3 \simeq R_3 \, C_3 \, l_n \, ((V_{CC} - V_{Tr})/(V_G - V_{Tr})) \qquad (3.9)$$

The impulse frequency is given as

$$f = 1/(T_1 + T_2 + T_3) \qquad (3.10)$$

For $V_G \leq V_{Tr}$, no impulses are generated, while as V_G approaches $V_{CC} - V_{CES}$ (the highest value of threshold), the impulse frequency reaches a maximum f –

$$f_{max} = 1/(T_1 + T_2) \qquad (3.11)$$

Fig. 3.10 gives an impulse frequency vs V_G plot. It is to be noted that the maximum threshold is finite ($V_{CC} - V_{CES}$) and for any input V_G above this value impulse generation will not take place as the comparator output will always remain high.

3.2.3 Active delay line

The axon may be simulated by an active delay line on which impulses propagate without attenuation. This may be achieved by several timers (using CMOS inverting gate) in cascade or sections of RC ladders with timers at the points corresponding to the nodes of Ranvier. Each timer may be used for a maximum delay equal to the pulse width.

CHAPTER IV

THE NERVOUS SYSTEM

In order to survive, the living organisms must adopt themselves to changing conditions. Higher organisms have developed a centrally controlled system which creates conditions favourable to the organism as a whole. There are usually several centres, with hierarchical relations among them. According to the manner in which signals are transmitted, two typical systems may be distinguished.

(a) The glandular system, where signals are transmitted through blood circulation system by chemical compounds.

(b) The nervous system, where signals are transmitted over nerve fibres by electrical pulses.

In addition to these systems, there are automatic regulation systems of individual organs. All these systems are interactive and a close cooperation between them forms the basis for survival. In this work, the interest is focused on the nervous system.

The nervous system is the supreme control organ and is found only in living organisms at higher stages of evolution. It processes an enormous amount of information obtained from the environment as well as from internal organs. In vertebrates, it is made up of the brain, the

spinal chord and the many nerve processes that pass between these two structures, as well as muscles, glands or receptors which they innervate.

There are several schemes of classifying the nervous system, the three possible bases for classification being the anatomy of the system, its function and an appropriate combination of the two. In one of these schemes[1] the brain and spinal chord together are termed as the central nervous system (CNS). The nerve processes outside it form the peripheral nervous system.

4.1 The Central Nervous System (CNS)

This is the supreme coordinating nervous system. It maintains the functional integrity of higher living organisms and controls their behaviour so that they are adapted to the given conditions in the most advantageous manner.

The simplest activity mediated by CNS is an elementary reflex which involves a receptor (sensory organ), afferent nerve fibres (transmitting sensory information to CNS), certain parts of CNS, efferent nerve fibres (transmitting control information from CNS) and an effector (executive or control organ). Reflexes can be classified from several points of views.[2,3] According to whether one is concerned with a contact with the environment of the

organism or its internal organs, reflexes are divided into somatic and autonomic ones. According to the part of CNS involved, they are divided into spinal and cerebral reflexes. According to whether they are acquired or innate, they are called conditioned or unconditioned reflexes. All the activities of CNS may be looked upon as a set of different kinds of reflexes, interacting with each other in a complex manner.

CNS can be roughly divided into seven basic parts[3-5]

(i) spinal chord

(ii) medula oblongatta (spinal bulb)

(iii) cerebellum (little brain)

(iv) mesen cephalon (midbrain)

(v) diecaphalon (between brain)

(vi) carpus striatum

(vii) cerebral cortex

These parts are in the order of both morphological and functional hierarchy.

Some lower control functions are directly performed by the spinal chord, whereas more complicated functions are left to the higher parts of CNS. In the spinal chord, all the reflexes without any exception, are unconditioned.

The spinal bulb performs some important functions - control of the action of blood circulation system, the respiratory control, the digestive system, defense reflexes, movement of facial muscles. It also plays important role on normal body posture. The little brain controls the coordination of more complicated movements. The midbrain mainly acts as an interface and in addition to it controls eye movements and mediates unconditioned auditory reflexes. The between brain has two parts - (a) Thalamus and (b) Hypothalamus. Thalamus processes all excitations resulting in various sensations (cerebral cortex also participates in them). Hypothalamus coordinates vegetative functions - blood circulation, temperature regulation, respiration etc. Corpus Striatum serves as a means of transformation, which controls the goal seeking function of skeletal muscles according to the orders from the cerebral cortex: Cerebral cortex performs all higher nervous activity. The fundamental element of cerebral cortex is conditioned reflex.

4.2 The Peripheral Nervous System

The nerve processes in the peripheral nervous system may be classified into afferent and efferent divisions. Cell bodies of afferent neurons are outside CNS. Regardless of whether the initial stimulus is picked up by exteroceptors (external sensors) or interoceptors (signalling internal

conditions), the action potentials travel along neurons which are structurally similar. These are also referred to as sensory neurons.

The efferent division may be subdivided into somatic and autonomic nervous systems. The somatic nervous system innervates skeletal muscles and the autonomic system innervates smooth and cardiac muscles and glands.

The cell bodies of the neurons in the somatic division are located in groups in CNS and the axons pass directly without any synapses to skeletal muscle. Their excitation always leads to a contraction of muscle cells, there being no inhibitory ones. These cells are also called motoneurons:

The fibres of the autonomic nervous system have synaptic interconnections in the intermediate region between CNS and the neuroeffector junctions. The autonomic nervous system can be further subdivided into sympathetic and para-sympathetic components.[6] They leave CNS at different levels and for most part are functionally reciprocal. The sympathetic nervous system tends to mobilise the body for emergencies, whereas the parasympathetic nervous system tends to conserve and store bodily resources.

4.3 Information Processing, Learning and Memory

Neurons encode the varying magnitudes of stimulus by the process of frequency modulation. This has a natural

immunity to noise. Although, the neuron is digital in action (action potential being all or none phenomenon), nature has discarded the much more efficient and compact positional number system in favour of the more primitive method of counting. The basic advantage of this is in the greater safety against errors and greater simplicity of encoding - decoding.[7] It also results in a large amount of redundancy.

Sensory organs supply CNS with a huge amount of information (according to some estimates - 10^9 bps) about the environment and internal state of the organism. It includes not only important, but also redundant information. CNS can not record and process such an amount of data. The sensory channels themselves encode these data, reducing the redundancy by filtering the parameters suitable for further processing. The processing inside CNS takes place at all the hierarchical levels.

Learning is a kind of plasticity of the nervous system. The nervous system, specially in mammals, can store information, can modify response to stimuli and can recover from certain irreversible structural damages. The processes of memory, logic and arithmatic involved are not well understood. Several theories relating learning to structural changes at the synapse or the chemical alterations within the nerve

cells have been proposed. However, the problem of total organisation of nervous system for memory and learning is unsolved. Theories of memory involving a physical change as the memory trace are of two sorts. Short term memory is explained in terms of active electrical processes, such as a reverberating circuit - a closed chain of neurons reactivating one another. Long term memory is thought to be the result of a more permanent alteration in brain chemistry or synaptic structure.[8,9]

CHAPTER V

THE CARDIOVASCULAR SYSTEM

The activity of the organs of cardiovascular system-the heart and the blood vessels , ensures a continuous flow of blood in the organism. Blood circulating in the organism performs a number of functions - gas exchange (supplying oxygen and carrying off carbon dioxide), nutrition of tissues, control of body temperature etc.

The flow of blood in the vessels is due to pumping action of the heart. As the requirements of blood for the entire body or its parts vary continuously, the heart and blood vessels are subject to continuous regulation in closed loops interconnected via the nerve centres.

5.1 The Heart

A simplified diagram of the human heart from an engineering point of view is given in fig. 5.1.[1] The right half of the heart pumps blood from the body into the lungs and the left half from the lungs to the body. These two subdivisions are called pulmonary or lesser and systemic or greater circulation respectively.

The structure of the two parts is the same - each consists of an atrium and a ventricle, separated by a valve which passes blood only from the atrium to the ventricle.

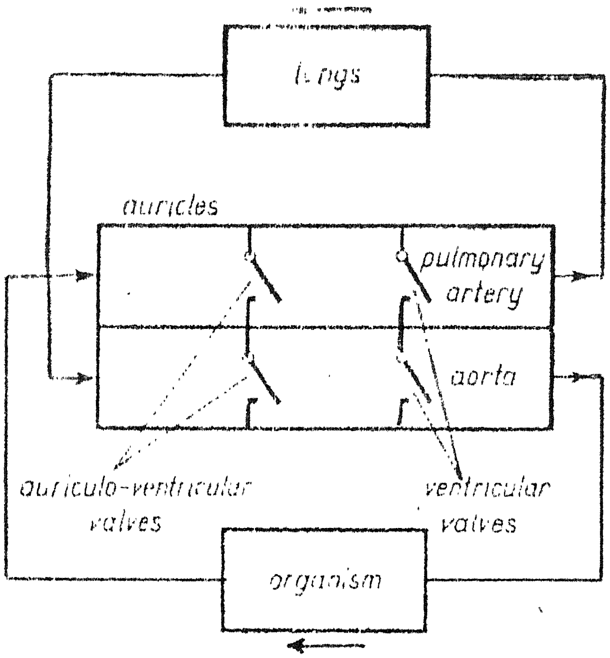


Fig. 5.1 A simplified diagram of the human heart

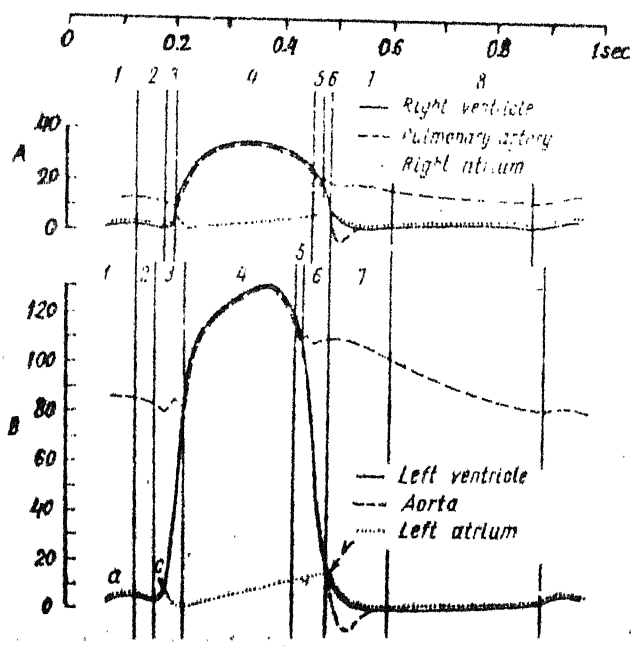


Fig. 5.2 Schematic representation of changes of pressure on (A) right and (B) left heat associated with the different phases of cardiac cycle (at 75 bpm.)

The outlet from the ventricle is also closed by a valve permitting only an outward flow of blood.

The rhythmic pumping of blood is performed by alternate rhythmic contraction (systole) and relaxation (diastole) of the muscular fibres that form the walls of the atria and ventricles. In normal physiological conditions systole and diastole occur in a definite coordination and constitute the cardiac cycle.[2] Fig. 5.2 shows the various phases of the cycle alongwith pressures, which will be discussed later.

Consecutive contractions of the heart follow each other because of the automatic mechanism of its own. The role of the nervous system is only in weakening or strengthening the heart action.

The automatic action is made possible by centres where self excitation occurs. These are the areas of muscular tissue of a special structure called nodes. The stimulation arises initially in the Sino-atrial (S A) node located in the front part of the right atrium near the orifices of venae cavac. This spreads through the muscles of atria in about 100 mS and reaches the atrio-ventricular (AV) node, the sole muscular connection between the atria and the ventricles. Upon passage through this node, excitation travels through specialised right and left bundles

and then through the arborised Purkinje fibres in about 100 mS. This system serves to initiate electrical activity in the ventricular musculature. The two ventricles contract simultaneously and the contraction persists for about 300 mS, normally followed by a relaxation period of 500 mS (with 75 beats per minute). The electrical conduction system is shown in fig. 5.3.[3]

The heart rate is basically determined by the activity in the SA node which operates, in a sense, as a free running multivibrator. The rate, however, is modified by the competing effects of sympathetic and parasympathetic nerves coming from CNS. The SA node is the main pacemaker of the heart. In the case of a failure of this main pacemaker, the AV node takes over the role of pacemaker and hence is known as the latent pacemaker. The contractions of the atria and ventricles may not then occur in their usual sequence, but almost simultaneously because stimulus from the AV node reaches the atrial and ventricular muscles almost at the same time. Ventricular contraction persists even after the A-V node has been separated from tho lower sections of the conduction system by ligation. The function of pacemaker is then performed by the Purkinje fibres lying in the right and left ventricles.

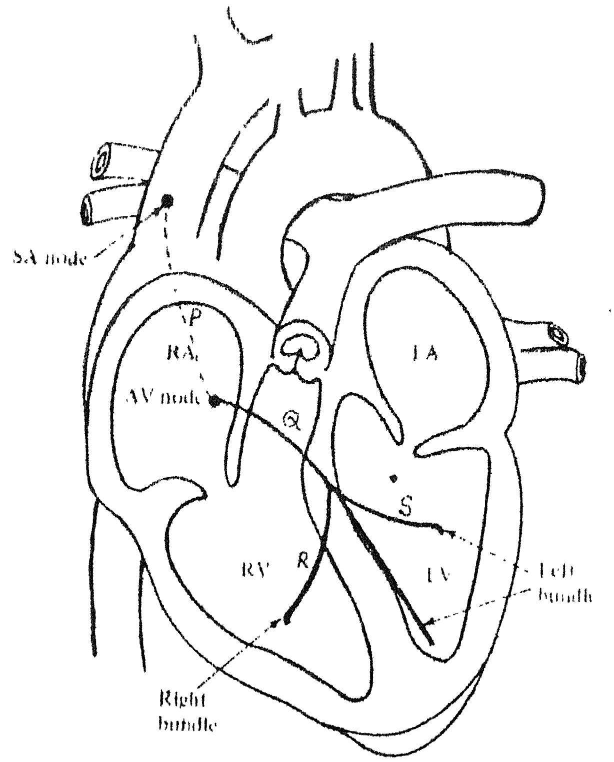


Fig. 5.3 Conduction system of heart.

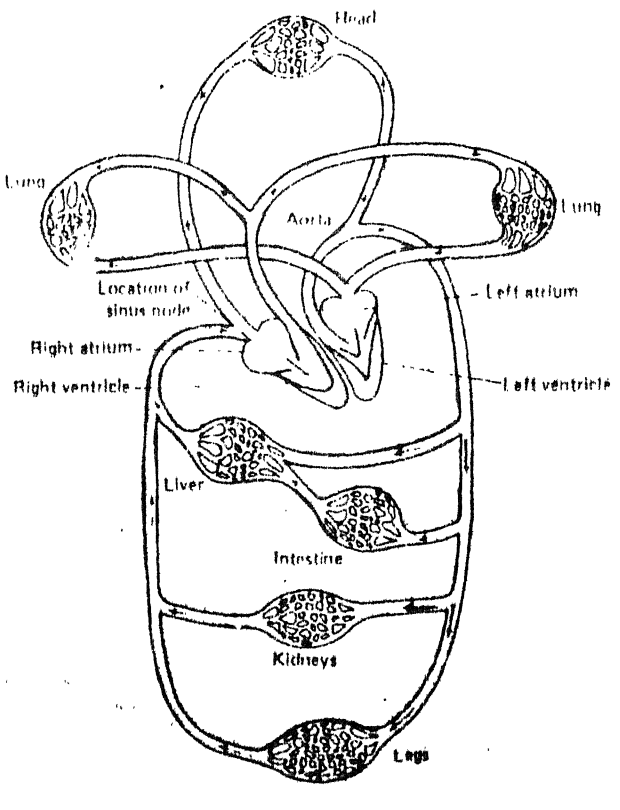


Fig. 5.4 Circulatory system.

The frequency of automatically originating impulses shows the degree of a pacemaker's activity. The rate of cardiac contraction in a normal man at rest averages 70 - 75 beats per minute (bpm). It changes with the physical activity due to actions of sympathetic and parasympathetic nerves and ranges from 60 to 85. With AV pacemaker, the rate is 40-50 bpm, while a heart working under the lower lying pacemakers contracts at an even slower rate (20-30 bpm).[4]

5.2 Disorders in Conduction and Heart Block

For proper functioning of the heart, adequate correlation between atrial and ventricular contractions is essential. This gets disturbed if the conduction of excitation is impaired.[5,6] This is referred to as a heart-block and may be due to congenital defects or accidental tissue damage.

An SA block is said to occur when SA node fails to initiate an impulse. When the conduction between the SA node ventricles is affected, it is called an AV block, which can be partial or complete. In a partial AV block, conduction from SA node to ventricles takes longer time or some impulses fail to reach the ventricles, while in a complete block, SA node impulses do not reach ventricles at all. Depending on the region in the conduction path (P,Q,R,S in fig. 5.3),

different kinds of disorders may be observed. When the section P is impaired, atria contract under the control of SA node, while ventricles contract under the control of AV node. There is a partial or complete dissociation between them depending on the degree of impairment. In case of failure of AV node itself or in the section Q, ventricles run under their own low-level pacemakers. Though the beat rate is low, the two ventricles remain in synchronism with each other. In another kind of disorder, one or both the branch bundles, (Section R and S) may be impaired. Impairment of both bundles results in the dissociation of the contractions of the atria, left ventricle and right ventricle.

The normal rate of heart rate varies from 60 to 85 bpm. However, sometimes a marked variation from this is observed. A lower beat rate (40-60 bpm) is known as brady-cardia and a higher beat rate exceeding 90 or 100 and some times reaching even 150 bpm is called tachycardia. Bradycardia is often observed in atheletes at rest, while tachycardia occurs during strenuous muscular work and in emotional shocks. A disorder leading to an irregularity of the rhythms is known as arrythmia.

Another serious kind of disorder may cause rapid and asynchronous contractions of the artrial or ventricular muscle fibres, reaching a rate of 400 bpm (flutter) or

600 bpm (fibrillation). With such fast asynchronous contractions the atria and ventricles cannot fulfil their function. Atrial fibrillation can persist for a long time without danger to life. The rhythm of ventricular contractions in this case is irregular because only a small fraction of the artrial impulses is passed from the atria to them. Ventricular fibrillation is fatal if immediate measures to stop this condition are not applied.

5.3 Blood Circulation

The actual physiological system for the heart and blood circulation system is shown in fig. 5.4. An equivalent diagram from the engineering point of view is depicted in fig. 5.5.[7]

The atria play the role of a reservoir that collects blood flouring from the veins during a ventricular systole. The blood passes from the atria to the ventricles during the ventricular diastole. The ventricles act as a pump that forces blood into the arterial system at relatively high pressure. The blood pressure in the atria, ventricle and artries under normal condition are shown in fig. 5.2.[8]

During atrial systole, the muscular constrictions at the entrance from veins contract so that blood flows from the atria only in the direction of the ventricles. As the

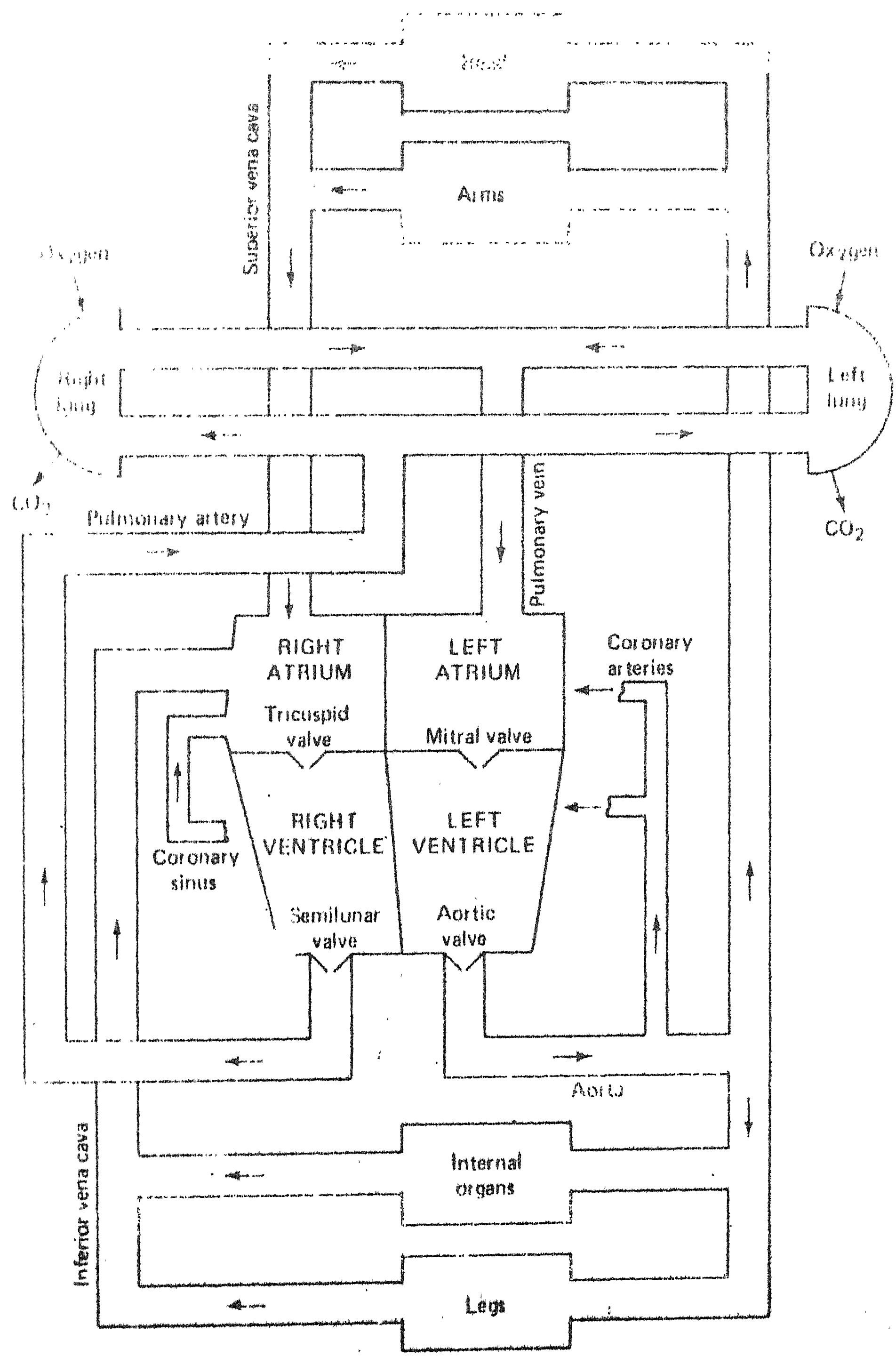


Fig. 5.5 Circulatory system - engineering point of view

ventricles are relaxed during the atrial systole and pressure within them is lower than that in the contracting atria, blood enters them from the atria. One way passage of blood from the ventricles into the main arteries is due to valves. The opening and closing of valves is conditioned by the blood pressures on the two sides.

The movement of blood in heart cavities and along the entire cardiovascular system is conditioned by pressure gradient and the resistance offered by pathways. The greater pressure developed in the left ventricles compared with the right is due to more powerful muscles of the former, which is associated with the fact that the left ventricle has to overcome a greater resistance to blood flow in the vessels of systemic circulation. The fluctuations of pressures in the aorta and pulmonary artery during the discharge of blood from the ventricles follow the changes of pressure in the corresponding ventricle. The form of the arterial pressure pulse changes as it passes through the arteries. The walls of the arteries cause damping and reflections. The flow of blood from the ventricles is in the form of pulse discharges. However, as the arteries branch out into smaller arteries with smaller cross-sectional area, the pressures and volumes change and the nature of flow changes. As the blood flows into the arterioles, the

pressure decreases and loses its pulsating character. As the blood returns to veinous system after travelling through capillaries, the pressure is down to about 15 mm Hg and finally in the veins returning to heart, the pressure is only about 2 mm Hg.

The systolic (maximum) and diastolic (lowest) pressures for clinical purposes are measured in the brachial artery in the arm. In a normal adult, the values are typically 120 and 80 mm Hg respectively. However, they are subject to variation with age, climate and other factors.

The quantity of blood discharged by the ventricle per minute is known as the cardiac output. The average value in a man at rest is 4.5 to 5 litres, corresponding to a complete turnover every minute. Cardiac output depends both on the stroke volume (blood discharged from ventricle with every beat) and the beat rate.

The minimum time required for the blood to complete both the systemic and pulmonary circulations is known as the total circulation time. The circulation time in humans is about 27 heart systoles. The actual time taken by the various possible circuits differ widely. It is due to the fact that the rate of flow along the walls of the blood vessel is lower than that along its axis and that extension of all the

vascular regions is not the same. The pulmonary circulation accounts for one fifth of the total circulation time.[9]

A normal blood supply to the organs and tissues requires a definite relation between the volume of the circulating blood and the total capacity of entire vascular system. This is achieved by several humoral and neural mechanisms. About 45 to 50 percent of all blood is accumulated in the so called blood reservoirs (the spleen, the liver, subcutaneous vascular networks and the lungs). These reservoirs play an important role in the regulation of blood flow. A redistribution of circulating blood occurs when an organ is working. Blood supply to the working organs is increased at the expense of decrease of the flow to other ones. The total volume of blood is maintained due to the continuous formation of blood cells and their destruction.[10]

5.4 Control of Cardiac Activity

The action of the heart, and the rate and force of its contraction vary with the activity of the organism and the various conditions in which it finds itself. Neural control is accomplished by impulses sent from CNS along the sympathetic and parasympathetic nerves.[11,12] They innervate the SA node, the muscle fibres of atria and the AV node. Impulses on the sympathetic nerve cause a more rapid

spontaneous depolarisation of the pacemaker cells during a diastole, which leads to the acceleration of heart contractions. The action due to parasympathetic nerves is the reverse. The nerve centres giving rise to these two nerves are in continuous excitation, called central tone. In the resting state, parasympathetic elements are dominant.

Reflex control of cardiac activity involves many nerve centres in CNS. The blood pressure is monitered at a large number of points through presso receptors which stimulate the different fibres. A higher arterial blood pressure causes increased impulse rate on them. This increases the tone of the parasympathetic centres, which makes the heart beat more slowly. A rise in the blood pressure in venae cavae gives rise to a reflex decrease in the tone of parasympathetic centres and to the stimulation of the sympathetic nervous system as a result of which heart beats faster and pumps more blood in the arteries from the veins and the pressure in the venae cavae falls. A difficiency of oxygen and other chemicals during physical exertion leads to stimulation of sympathetic centres which leads to increase in cardiac activity.

In addition to nervous control, cardiac activities are influenced by humoral controls and many other factors such as temperature etc.

CHAPTER VI

SIMULATION OF THE CARDIOVASCULAR SYSTEM

Simulation of the cardiovascular system consists of the simulation of two distinct mechanisms (i) conduction of excitation in heart and (ii) blood circulation and various related processes.

6.1 A Simple Simulation of the Conduction System

The simplest simulation of the cardiac output and its effect is just a charge pump as shown in fig. 6.1. As the activities of different chambers of the heart are not distinguished in this model, this allows the simulation of conduction of electrical excitation in terms of three distinct pacemaker activities in the heart, as follows

(i) A controlled oscillator representing the SA node - The autonomic nervous system (ANS) controls the running frequency by two control inputs sent through the sympathetic and parasympathetic nerves.

(ii) An oscillator representing the AV node - The free running frequency is lower than that of the SA node. Under normal conditions, pulses from the SA node synchronise the AV node oscillator to the same frequency as that of the SA node.

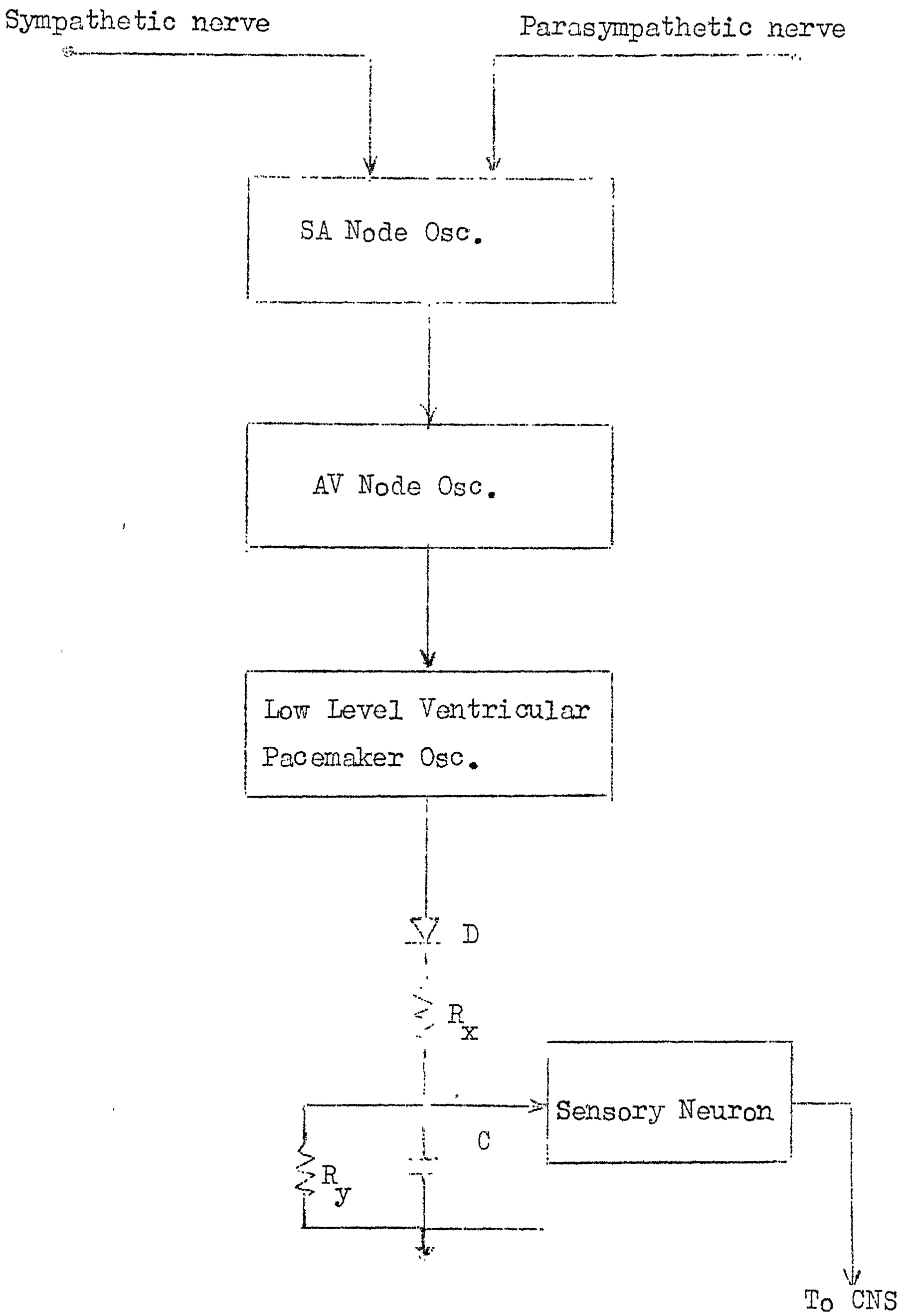


Fig. 7.1. A simple simulation of cardiac activities

(iii) An oscillator representing low level pacemakers in ventricles. In the event of an AV block, it runs at a low frequency as a free running oscillator. Under normal conditions of AV conduction, this oscillator is synchronised with the higher pulse rate of the AV node oscillator.

The output of the ventricular oscillator drives the charge pump and there is a release of certain charge on the capacitor C corresponding to the heart output with each beat. A leakage resistance R_y across the capacitor simulates the diffusion of blood. The voltage across the capacitor may be taken as a measure of cardiac activity and fed to CNS through a sensory neuron.

6.2 Simulation of the Circulatory System

The simple model of fig. 6.1, exhibits the three levels of automation in the excitation system. But in order that any simulation be really meaningful, it must include some kind of simulation of the circulatory system as well. An electrical simulation can be developed using the following electrical analogues for hydraulic parameters -

(a) pressure - voltage

(b) flow - current

(c) volume - charge

With these analogues, the friction in blood vessels may be modelled by resistance; the capacity of a part by capacitance and compliance by inductance. In the heart, opening of a oneway valve is decided by the differential pressure across the valve, which may thus be represented by a diode.

For the sake of a meaningful yet reasonably simple simulation, the following assumptions and approximations have been made -

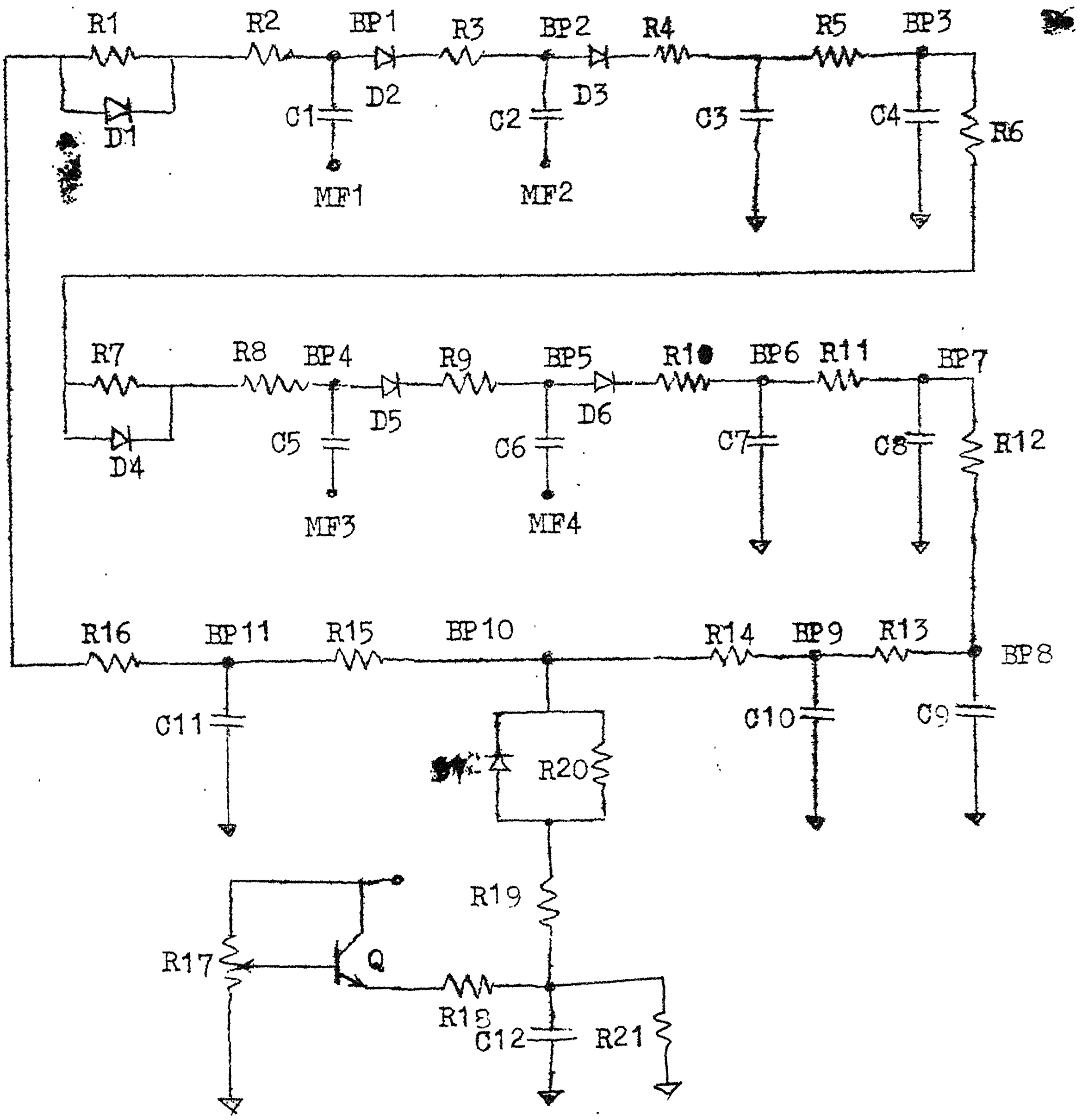
(i) The circulating fluid (blood) has no compliance. Thus no inductors are included in the simulation.

(ii) The entire region of any of the heart chambers contracts or expands simultaneously(in contrast to the actual case of propagation of contraction wave).

(iii) The stroke volume is constant (in contrast to the variations in stroke volume in accordance with the needs of the body.

(iv) The distributed circulatory system can be represented by a finite no. of sections.

A simulation of the circulatory system has been developed as shown in fig. 6.2. The contractions of various chambers are simulated by pulse drivers with outputs in correspondence with the actual forces of contraction. The muscular constriction



R1 -1M, R2-1.5K, R3-1.5K, R4-12K, R5-12K,R6-12K,R7-1M,R8-1.5K,
R9 -1.5K,R10-15K, R11-15K,R12-15K,R13-15K,R14-15K,R15-15K,R16-15K,
R17-50K, R18-100K,R19-680K,R20-680K,R21-1M,Q-BC147,C1-C11=10μf poly.
C12-10μf electrolytic

D1,R1-Muscular constriction at the entrance to right atrium.
R2,C1- Right atrium. D2-Tricuspid valve. R3,C2-Right ventricle.
D3-Semilunar valve. R4,C3,R5,C4,R6-Pulmonary circulation.
D4,R7-Muscular constriction at the entrance to left atrium.
R8,C5-Left atrium. D5-Mitral valve. R9,C6-Left ventricle.
D6-Aortic valve. R10,C7,R11,C8,R12,C9,R13,C10,R14,R15,C11,R16-
Systemic circulation. R17,Q,R18,R19,R20,D7,C12,R21-Regulating
Reservoir.

Fig. 6.2 Simulation of circulation system

at the inputs to the atria are represented by diodes shunted by resistors. The pulmonary circulation is represented by two sections of R-C ladders, while systemic circulation is represented by five such sections.

Before the last section of systemic circulation a regulating reservoir has been introduced. Its function is to regulate the amount of charge (blood) in circulation. It incorporates the functions of blood reservoirs and the organs taking part in continuous formation and destruction of blood cells.

Effects of bleeding as well as transfusion can be simulated by leaking the charge or introducing the charge somewhere in the circulatory system.

6.3 A Detailed Simulation of Conduction System

In view of the model of the circulatory system proposed in the preceeding section, certain features have to be incorporated in the simulation of conduction system so as to make them compatible with each other. For the sake of avoiding complexity, the various pacemakers are treated as localised points (which is justified because in the simulation of circulation, propagation of the contraction wave in the chambers of heart has not been considered). Further the effects of

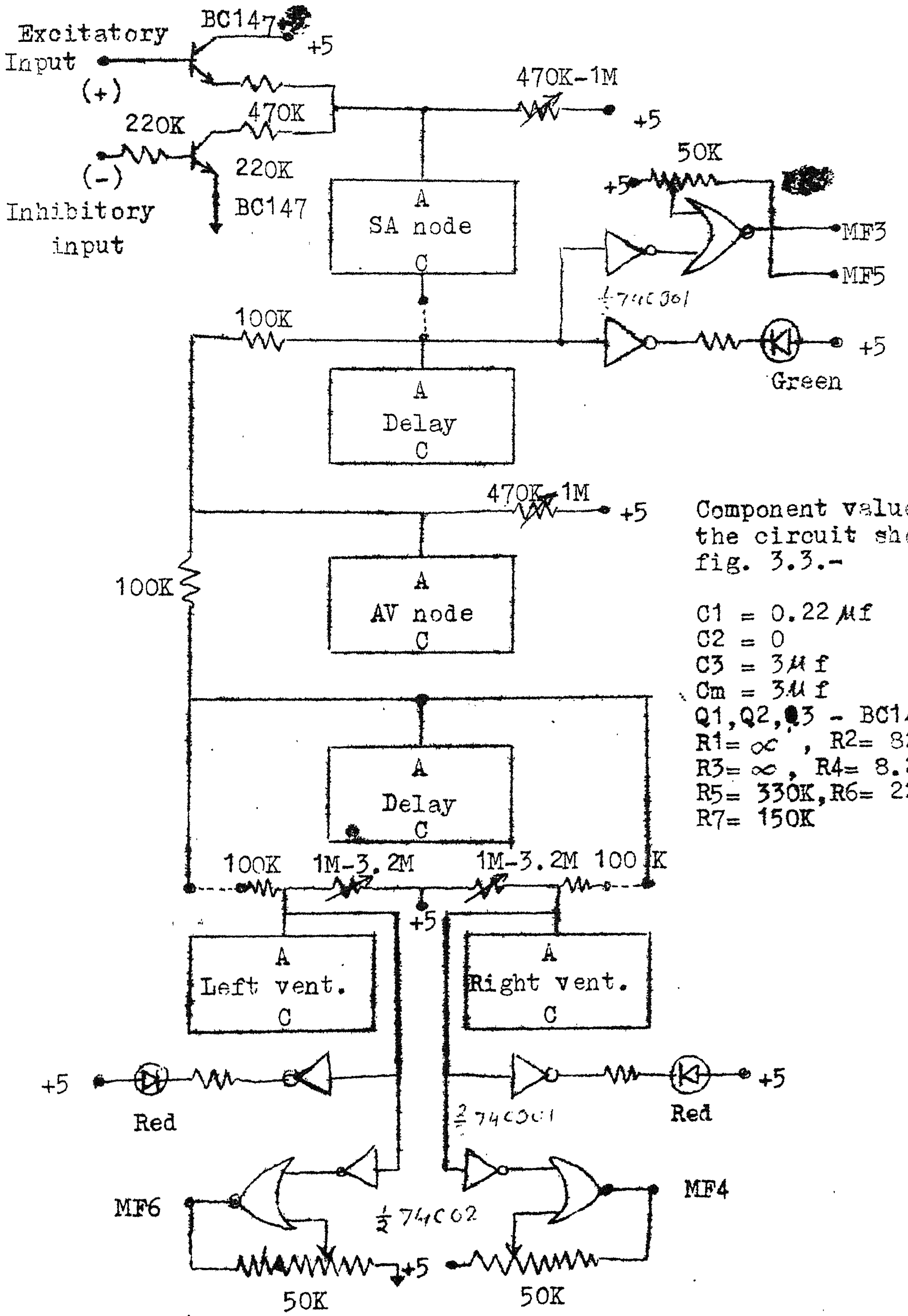
sympathetic and parasympathetic nerves in the autonomic nervous system is assumed to have effects on SA node only. Thus the simulation has to incorporate the following features -

(i) Separate pacemaker activities of the two ventricles.

(ii) Bidirectional paths envolving certain delays between the various nodes, which would allow proper conduction among the contractions of the various chambers.

For simulating the various node oscillators as well as delay paths between them the circuit shown in fig. 3.3, proposed for simulating the membrane patch has been used. This relatively simple circuit features an absolute refractory period and can be made self oscillatory by increasing the resting value of V_m above the threshold, which can be readily accomplished by connecting a resistor from the supply to the input. By changing this bias, different free running frequencies, corresponding to different nodes may be achieved. For the bidirectional delay paths between them, same circuit with no self excitation has been used. The whole conduction system is thus simulated as shown in fig. 6.3.

The excitatory and inhibitory controls on the SA node activity have been simulated by adding two transistors Q_1 and Q_2 to the basic circuit. Each impulse on the sympathetic nerve



Component values for the circuit shown in fig. 3.3.-

C1 = 0.22 μf
C2 = 0
C3 = 3μf
Cm = 3μf
Q1,Q2,Q3 - BC147B
R1= ∞ , R2= 82K,
R3= ∞ , R4= 8.2K,
R5= 330K, R6= 22K,
R7= 150K

Fig. 6.3 Simulation of conduction system

For simulating the different forces with which the muscles of different chambers contract, the pulse heights to the inputs of the capacitors (representing the heart chambers) have been made adjustable. As the two atria do not have separate pacemakers, normally there is no conduction disorder and there is not much of difference of contraction forces of the muscles, a single output from the point before the delay between SA and AV nodes, has been taken to represent the muscle forces of both the atria. The two ventricles have distinct paths of conduction from the AV node (the left and right His bundles), different forces of contraction and separate low level pacemakers. All these features are incorporated in the simulation.

6.5 Feedback to CNS

The two kinds of parameters related to the cardiovascular activities, which are sensed and feedback to CNS are -

(i) Pressure levels at different points in the circulation system,

(ii) Levels of oxygen as well as various chemicals required for metabolism in the tissues.

As it is not possible to include anything analogous to the level of oxygen and various chamicals in the charge, the analogue for blood, we assume that these levels are constant, thus ignoring the effects of variations in breathing and

various humoral processes. The reserve of oxygen and other vital chemicals is modelled by the charge on the capacitor C in a charge pump as shown in fig. 6.4. The flow rate is sensed by sensing the voltage across a resistor in the circulation path. In order to avoid Op Amps, the difference amplifier has been made using CMOS inverting gates (vide-Appendix) with transistor buffers at the inputs, although it does have a finite leakage current leading to drift. A charge proportional to the flow rate is released on the capacitor C, the voltage across C representing the level of the reserves and this can be fed to CNS through a sensory neuron.

The effects of physical exertion, resulting in depletion of the reserves is simulated by a variable leakage resistance across C.

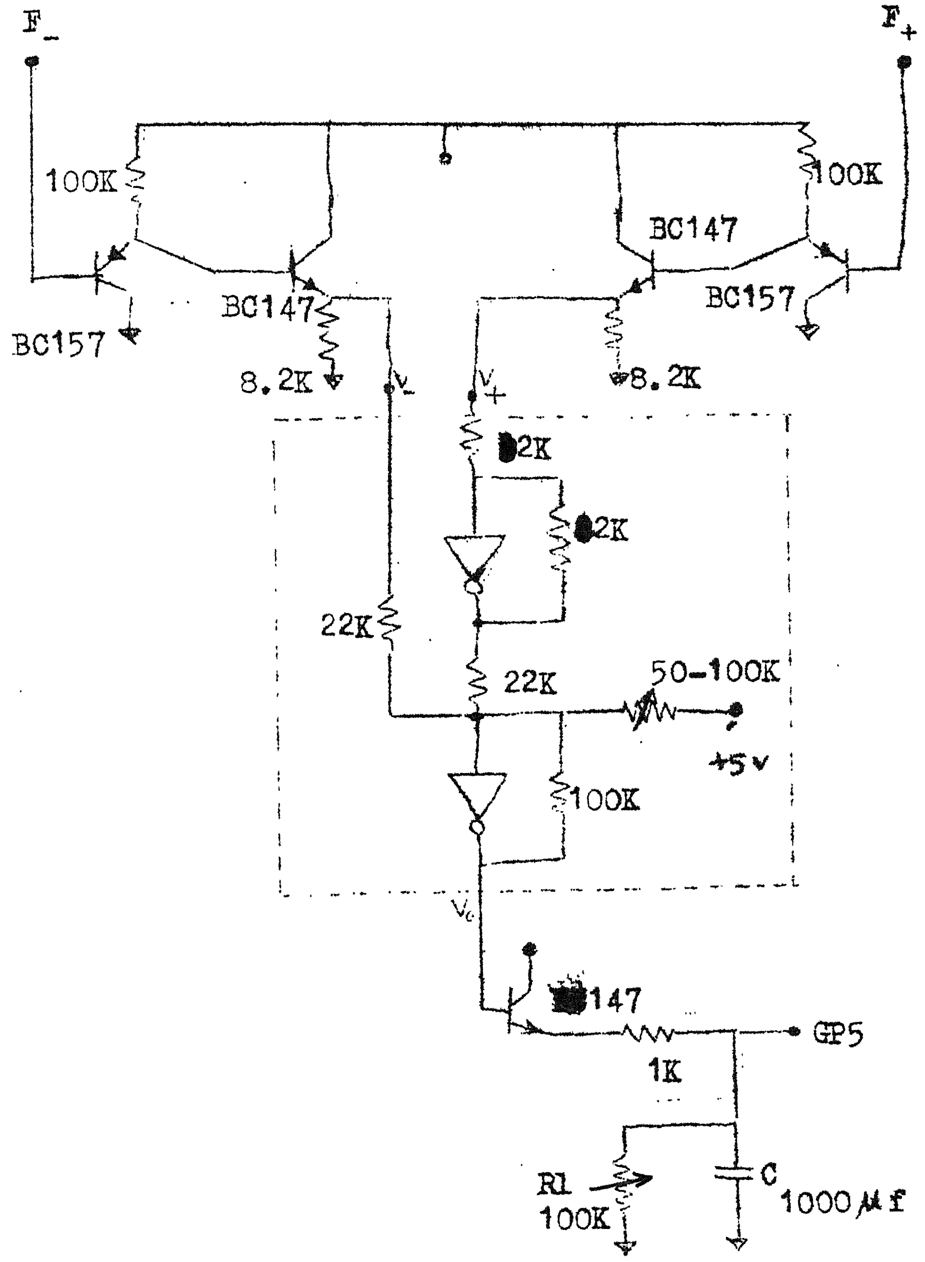


Fig. 6.4 A simulation of oxygen and chemical reserves

CHAPTER VII

SIMULATION OF THE NERVOUS SYSTEM

The processes involved in the peripheral nervous system may be simulated by using receptor models and a suitable interconnection of neural cell models. Simple unconditioned reflex involving spinal chord can also be simulated with one or more synaptic junctions in the spinal chord.

It is possible to achieve the processes of logical functions and short time memory by using simple neuron models.[1,2] However, the approach involves a tremendously large no. of neuron cells to exhibit any kind of conditioned reflex activity or learning process. Therefore, in the present work higher activities of CNS have not been simulated by using a neural net, but a microprocessor based system has been used instead. This allows one to use the same hardware for simulating various kinds of conditioned reflexes and learning processes simply by making appropriate changes in the software.

For the peripheral nervous system the neural cell model discussed in chapter 3 has been used as a basic module.

7.1 The Brain Simulation

The brain simulation has been realised with a microprocessor system with several input ports (simulating afferent

division) and output ports (simulating efferent division). The processor is connected to a RAM, which serves as a memory during processing and a ROM, which stores the program for simulating the various processes.

Because of the processing time involved and the hardware considerations, the no. of afferent and efferent nerves was restricted to six and four respectively.

A general picture of the organisation is shown in fig. 7.1.

The processor handles the ports and does the processing in real time with the help of a timer. The timer keeps interrupting the processor at certain regular intervals (cycle-time). After each interrupt, the processor reads the data from the input ports, does the processing, serves the output ports and then goes to a wait loop, a similar cycle is initiated by the next interrupt.

Due to the availability of various software development facilities and support chips, the processor chosen is Intel 8085. It is operated at 2.5 MHz clock (provided by on the chip clock generator and an external 5MHz crystal).

7.1.1. Input interface

Since Intel 8085 is a parallel 8-bit processor, the impulse rates on the afferent channels have to be converted

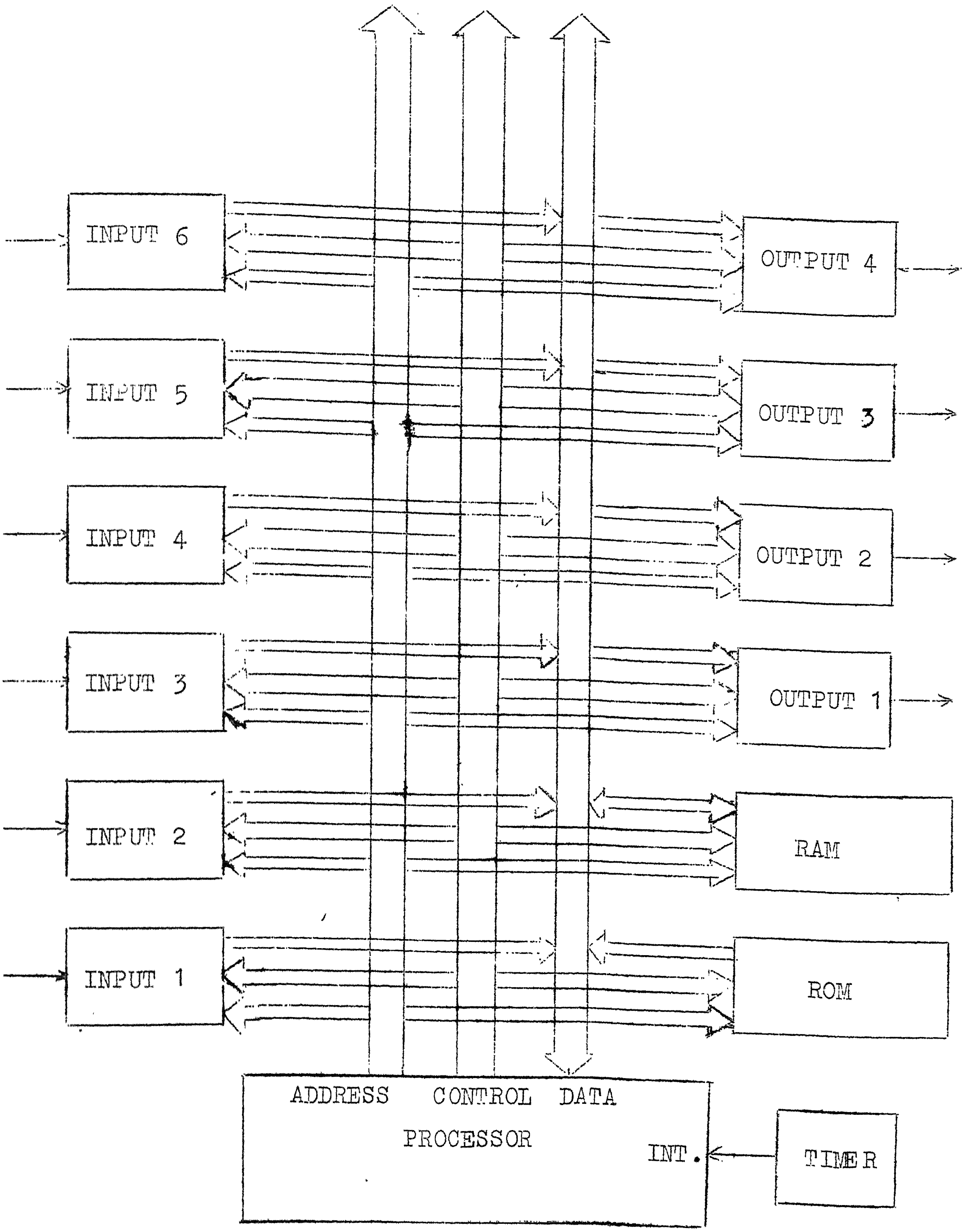


Fig. 7.1 A general organisation of a microprocessor based simulation.

to an 8-bit parallel data word. This has been achieved by giving the impulses on the channel as a clock to an 8-bit counter. The counter output is read by the processor as the strength of the signal on the channel and the counter is cleared for accumulating the counts in the next time slot.

7.1.2 Output interface

The output on each efferent channel also has to be in the form of of a series of impulses; the frequency being proportional to the signal strength. This has been achieved by using an 8-bit pulse rate multiplier (PRM). The output data is latched onto the PRM input and a clock derived from the system clock is given as the PRM clock.

7.1.3 Cycle time

In choosing the cycle time, one has to make a compromise between the temporal resolution of sensory signals and the complexity of the learning processes that can be simulated. A value of 100 ms has been chosen, as a value higher than this may result in unacceptable loss in time resolution. However, this interval is decided by a software controlled timer (on Intel 8156 chip which also provides 256 bytes of RAM and 2 output ports) and one has the option of choosing his own cycle time by modifying the setting of the timer.

7.1.4 Memory & I/O map

A direct I/O scheme has been chosen. A circuit diagram of the system has been shown in fig. 7.2. The memory and I/O map is given in Table 7.1.

TABLE 7.1

(A) Memory map - ($IO/\overline{M} = 0$)

Address (Hex)	Selected Device	Remarks
0000 - 07FF	2716 (EPROM)	AD_{0-7} is latched using ALE to provide A_{0-7} for 2716. D_{0-7} of 2716 is connected directly to AD_{0-7} of 8085
0800 - 08FF	8156 (RAM)	AD_{0-7} and all controls of 8156 are connected to the corresponding lines of 8085

(B) IO map - ($IO/\overline{M} = 1$)

Port Address (Hex)	Port Assignment	
0	Input port 1	(S1)
1	Input port 2	(S2)
2	Input port 3	(S3)
3	Input port 4	(S4)

4	Input port 5 (S5)
5	Input port 6 (S6)
6	Output port1 (M1)
7	Output port2 (M2)
8	CTR of 8156
9	Output port3(C1)-PA of 8156
A	Output port4(C2)-PB of 8156
B	Unused
C	Lower timer byte of 8156
D	Higher timer byte of 8156

7.1.5 Program structure

The program of the software to be loaded in 2 K ROM should have following structure -

(1) INITIALISATION - The timer and I/O ports of 8156 are programmed. Various registers and RAM locations are cleared or set as desired by the programs.

(2) WAIT - A wait loop. The processor remains in the loop until a hardware interrupt on RST 7.5 (sent by the timer) is received and goes to the processing routine RS75.

(3) RS 75 - Service the I/O ports and do the processing. After completion of the processing processor goes back to the wait loop in (2). The total time taken by the routine must be less than the cycle time.

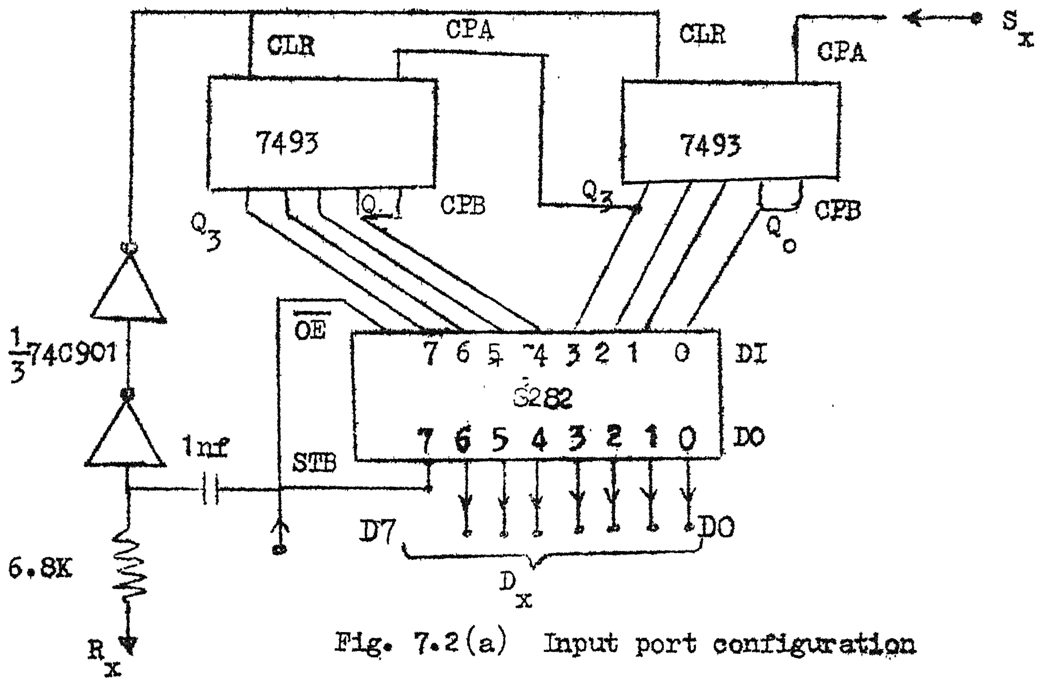


Fig. 7.2(a) Input port configuration

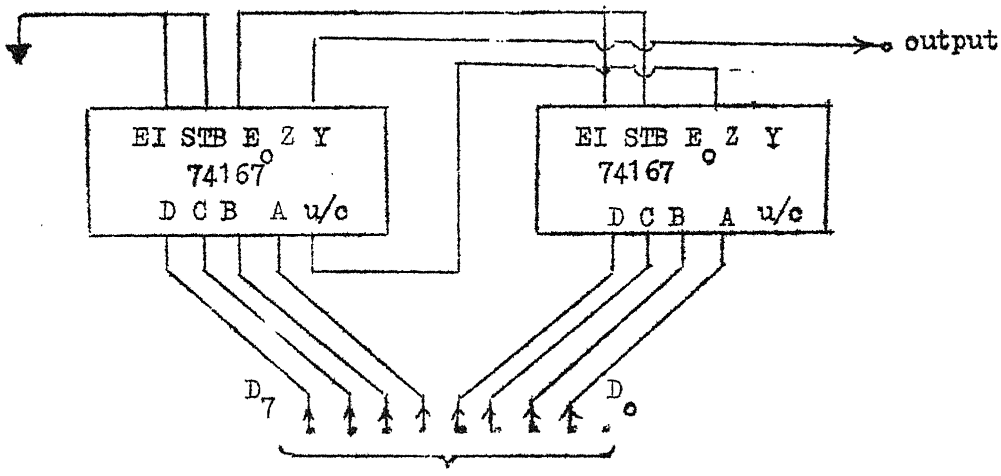


Fig. 7.2(b) 8-bit PRM in output port

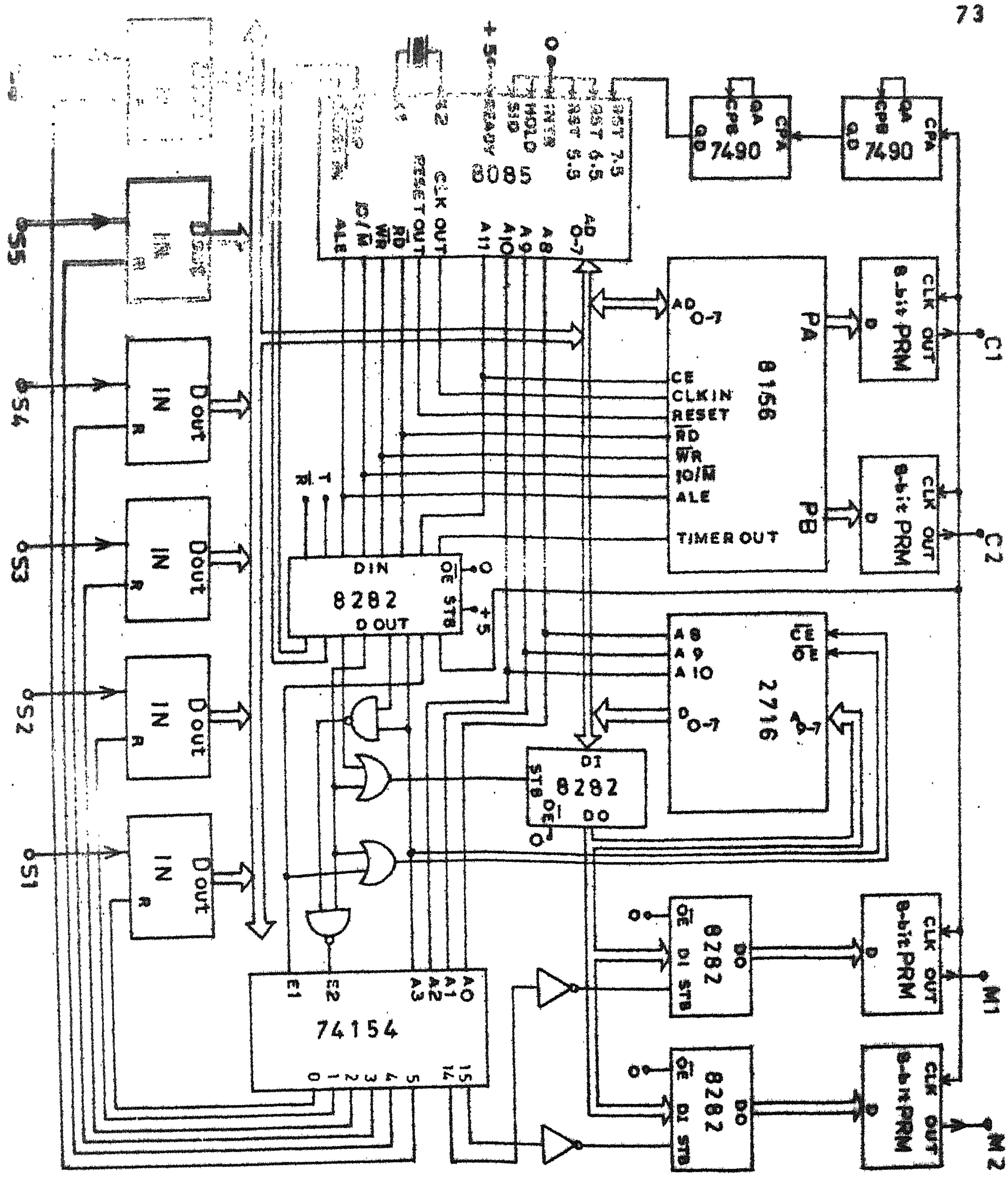


Fig. 7.2 c Microprocessor based system for 'brain' simulation.

(4) TRAP - Whenever unmaskable hardware interrupt TRAP is received, it indicates a catastrophic situation and the processor immediately starts executing this routine. Processor may return to normal mode after TRAP line goes low.

7.2. Peripheral Nervous System Simulation

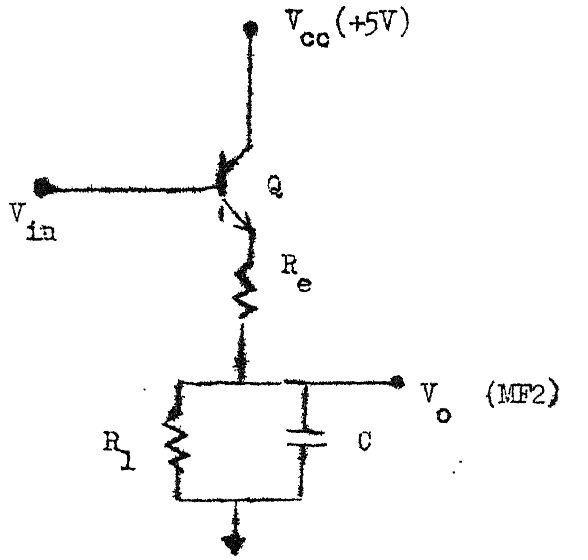
For simulating the afferent division of peripheral nervous system, the model developed for a nerve cell in section 3.2 has been used. However, the axonal delay simulation has been omitted because for simulating any reasonable amount of delay, a large number of timers are needed and it is really of not much consequence from the point of view of simulation.

The first two sensory channels have one excitatory input each. The third channel has one excitatory and one inhibitory inputs, while fourth channel has one inhibitory and two excitatory inputs.

The remaining two channels do not have the generator potential block, i.e. analogue processes, viz - adaptation, temporal and spatial summation etc. are not incorporated. These are suited for sensing the internal parameters, viz - blood pressure and the level of reserves of vital chemicals. An unconditioned spinal reflex has been incorporated by a synaptic

function after the first cell (corresponding to a synapse in the spinal chord) which excites a motoneuron (only the action potential block).

The efferent division of PNS has five members. Two of the outputs from the 'brain' form the autonomic division and control the cardiac activity by innervating the SA node. The other two outputs from the 'brain' and the motoneuron output in the spinal reflex form the somatic division. In actual case one motoneuron excites many muscle fibres, the response of individual fibres being on all or none principle. The effect is the result of the fact that a particular muscle is excited by a large no. of nerve fibres. In the present case, the interest is in seeing the effect of change in impulse rate on a motoneuron, over a muscle output and therefore, in place of simulating individual fibres, a circuit which converts the impulse rate to a corresponding dc level (shown in fig. 7.3) has been used. There are two such muscles. One is excited by the spinal reflex as well as one output involving brain, and by breaking the paths; effects of spinal reflex may be seen. The other one is excited by the output involving brain only.



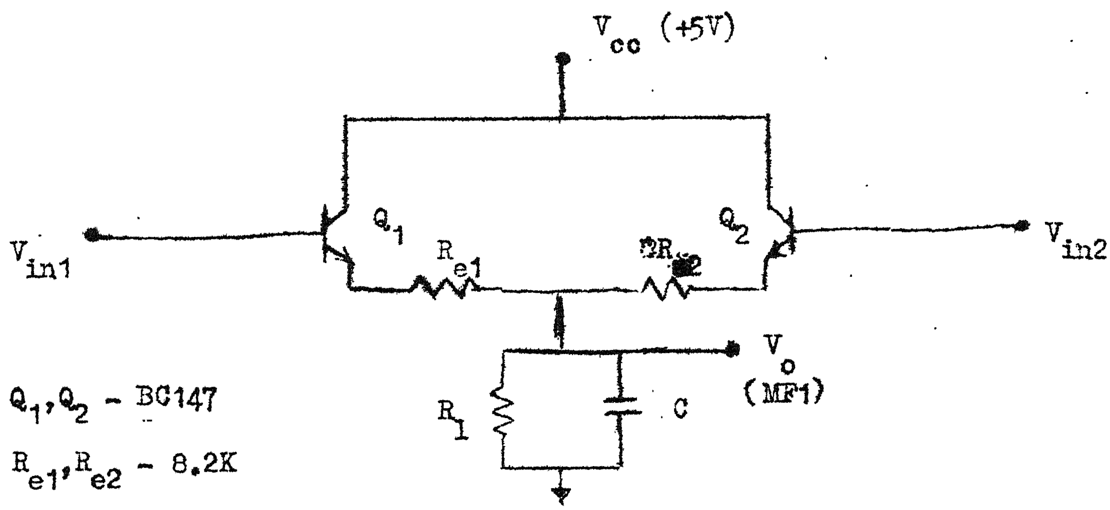
Q - BC147

R_e - 8.2K

R_1 - 100K

C - 10 f

(a) Muscle with one excitation input



Q_1,Q_2 - BC147

R_{e1},R_{e2} - 8.2K

R_1 - 100K

C - 10 f

(b) Muscle with two excitation inputs

Fig. 7.3 Muscle Simulations

CHAPTER VIII

SYSTEM ORGANISATION AND OPERATION

The simulations of nerve cells, the cardiovascular system and the nervous system as developed and discussed in chapters III, VI and VII have been made to form a system, which may be used to perform a variety of experiments. In this chapter an overall organisation, printed circuit card details, operating details and suggested experiments are presented.

8.1 Overall Organisation

The system has been made in three cards - (i) CNS (brain) simulation, (ii) cardiovascular system simulation and (iii) the peripheral nervous system (PNS) simulation (alongwith muscle simulations and one spinal reflex involving a synapse).

As the simulation of CNS is based on a microprocessor, the internal signals are of little interest from the bioelectric point of view. Hence for the sake of simplicity, all the data, control and address buses have been kept internal to the card. The external connections to the card consist of the power supply lines, six serial input lines (afferent nerves S1-S6), four serial output lines (efferent nerves: M1,M2,C1,C2) and two system control lines (RESET and TRAP).

The PNS and cardiovascular system simulation cards are both mounted on the back of the front panel, with PC test pins coming out through holes in the panel. The various points of interest have been made easily accessible to the user through these pins. The cardiovascular system simulation card has only the power supply connections while the PNS simulation card has twelve lines from the CNS card (S1-S6, M1, M2, C1, C2, TRAP, RESET) also connected to it through a connector. There is a set of potentiometers and jacks on the panel which have been provided for different purposes. The whole set up is such that all the cards and the panel may be easily separated.

The entire organisation of the system is printed on the front panel, shown in fig. 8.1. The internal connections between various blocks are shown by solid lines, while the ones to be made by the user are suggested by dotted lines. All input points use black pins, while output points use red pins. In cases where one may be interested in seeing the signals even after making the external patch card connections, additional test pins (blue) have been provided .s they are in parallel with corresponding output pins in many cases, one should be careful in using any of such points as inputs. Grey pins have been used for accessing signals representing the blood pressure in the circulation system and the forces of contraction of cardiac musculature. The monitoring of blood pressures should be done using high impedance probes.

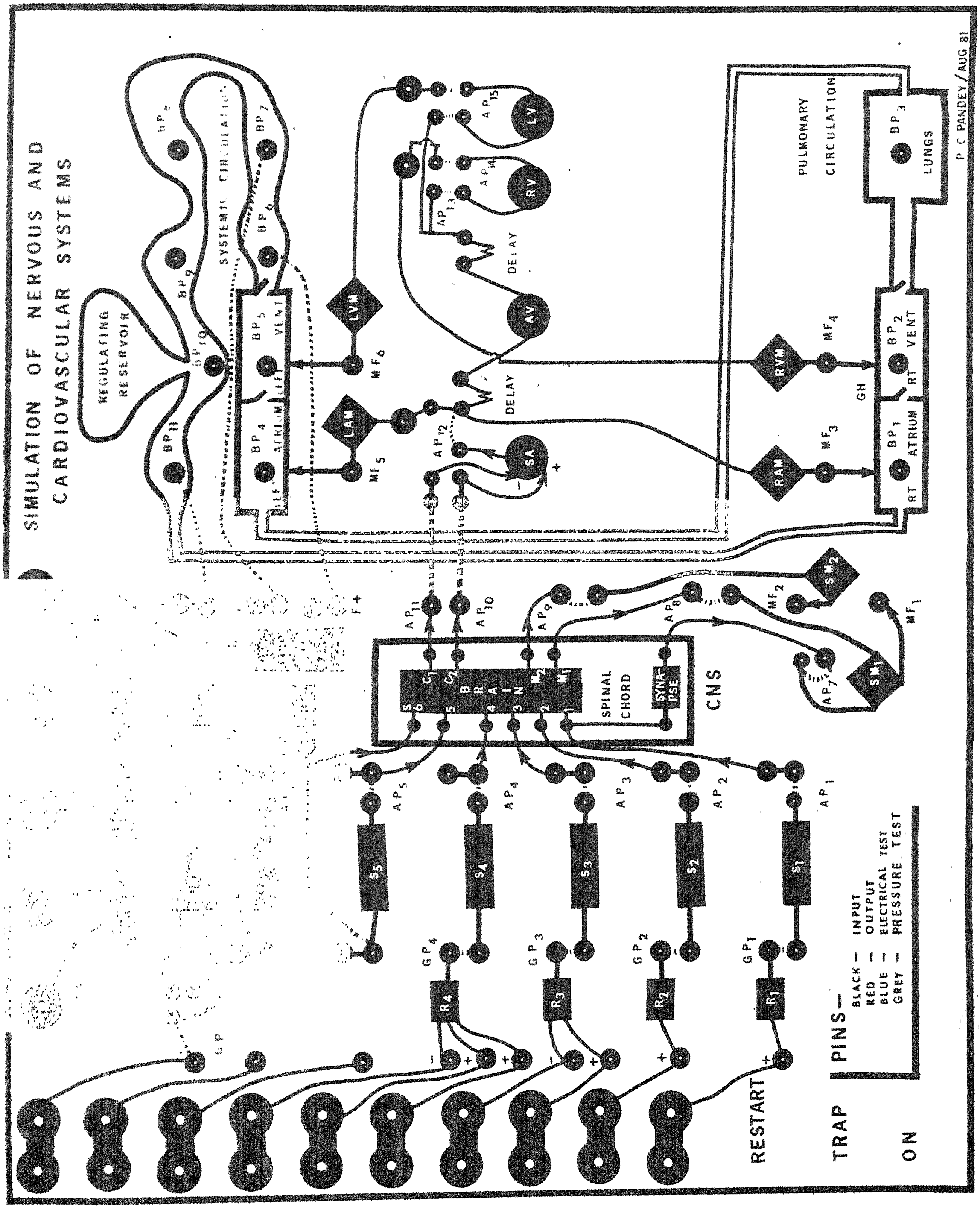


FIG 8.1 FRONT PANEL

8.2 PC Card Details

The details of the three PC cards are discussed in the following subsections.

8.2.1 CNS Card

The schematic of the circuit on this card is given in fig. 7.2. The functions of various components are listed in table 8.1.

Table 8.1

List of functions and nos. of components on CNS card (PC 1

Components	Functions	Nos.
1) Intel 8085	8-bit microprocessor	1
2) Intel 8156	256-byte of RAM, two 8-bit output ports and one programmable timer	1
3) Intel 2716	2K byte EPROM	1
4) Intel 8282	(a) 8-bit latch/tri-state buffer at input ports	6
	(b) 8-bit latch at output ports	2
	(c) 8-bit buffer for control lines	1

	(d) 8-bit address latch/ output data buffer	1
5) 7400	Two NAND gates used in the decoder logic and two inverting gates used for strobing output latches	1
6) 7432	Two OR gates used in the decoder logic	1
7) 7490	Decade counter. Two of them have been used in cascade to get the interrupt clock from 8156 timer	2
8) 7493	4-bit binary counter. Two of them have been used to make an 8-bit counter in the input port	12
9) 74154	I/O decoder	1
10) 74167	4-bit BCD PRM. Two of them have been used for 8-bit BCD PRM in the output port	8
11) 74C901	Hex inverter. Two inverting gates have been used in deriving the 'clear' pulse from the input port 'read' line. Thus one chip serves three ports	2

12)	5MHz X-tal	Crystal for on the chip clock generator of 8085	1
13)	1 nf cer disc cap	Used in generating the 50 μsec clear pulses to the counters in	6
14)	6.8K res.	input ports	6
	0.1 μf cer disc cap	Decoupling capacitors (distributed on the card)	25
15)	1000 μf electrolytic cap	Filtering capacitor at the V_{cc} pin	1

There are two V_{cc} lines coming from the card with a current requirement of about 1A on each. The PC layout of the card is given in fig. PC1 (appendix).

8.2.2 Cardiovascular system card

The PC layout of the card is given in fig. PC2 (appendix). This card contains the circuit simulating the cardiac conduction system and the circulation system. The contraction of chambers are indicated by LED s fixed on the card and coming out of the panel. The circuit (alongwith component values) for circulation system and conduction system have been given in fig. 6.2 and fig. 6.3 respectively. The current requirement of the card is about 100 mA.

8.2.3 PNS card

The PC layout of the card is given in fig. PC 3 (appendix). There are six sensory channels forming the afferent division of PNS. For observational convenience and flexibility the receptor and action potential blocks have been made separately and the external patch chord connection is suggested by the dotted lines. R1 - R4 are the receptor cells or the generator potential blocks. The circuit has been shown in fig. 3.6. They incorporate the features of adaptation and spatial and temporal summation. The component values (ref fig. 3.6) are given in table 8.2.

Table 8.2

Component values in the receptor cells

Cells	No. of excitatory inputs	No. of inhibitory inputs	Components
R1	1	0	R_1-180K, C_1-10 μf R_2-330K, R_3-1.5 K R_4-15K, C-10 μf Q - BC 147
R2	1	0	R_1-180K, C_1-10 μf R_2-680K, R_3 - 1K R_4- 15K, C-10 μf Q - BC 147

R3	1	1	R1-180K, C_1-10 μf R_2-680K, R_3-1K R_4-15K, C-10 μf Q - BC 147 R_1'-180K, C_1'-10 μf R_2'-680K, R_3'-1 K R - 100K, Q'-BC157 Inverting gate - 74C901/6
R4	2	1	R_1-150K, C_1-10 μf R_2-680K, R_3-1.8K R_4-22K, C- 10 μf Q - BC 147 R_1'-150K, C_1'-10 μf R_2'-680K, R_3'-1.8K R- 100K, Q'-BC 157 Inverting gate- 74C901/6

S1 - S6 are action potential blocks with the circuit shown in fig.3.9. This circuit has also been provided on the card with the provisions of parameter variation. The panel shows the internal blocks of this circuit. The resting threshold, threshold decay rate, pulse width and absolute refractory period can be controlled using variable resistances provided on the panel. We refer this block as S. There is a simulation of a spinal reflex incorporating a synapse and a motoneuron. The motoneuron also has been simulated by the circuit in fig. 3.6. The component values for S1-S6, S and MN the motoneuron in spinal reflex are given in table 8.3.

Table 8.3

Component values in S1-S6,S,MN

Component	R (K)	R1 (K)	R2 (K)	R3 (K)	R4 (K)	RB (K)	C1 (pf)	C2 (pf)	C3 (f)	Q	Inverting gates
S1 - S4	100	51	51	15	00	100	10K	10K	0.47	BC157	74C901
S5,S6	100	51	51	6.8	00	100	10K	10K	0.47	BC157	74C901
S	100	6.2-220	6.2-220	15-82	18-∞	100	10K	10K	0.22	BC157	74C901
MN	100	51	51	15	00	100	10K	10K	0.47	BC157	74C901

Measurement results for S1, S5 and S are presented in table 8.4 and pulse repitition frequency VS input voltage plot for S1 is given in fig. 8.2.

Table 8.4

Measurements on S1, S5 and S

(A) T1,T2

Block	S1	S5	S
T1(ms)	0.59	0.50	0.1 - 2.3
T2(ms)	0.45	0.45	0.5 - 2.5

(B) Time period T and prf f for S1 and S5

Input voltage V_i (v)	T(S1) (ms)	f(S1) (Hz)	T(S5) (ms)	f(S5) (Hz)
0.5	27.6	36.2	9.4	106.3
1.0	15.0	66.6	6.5	153.8
1.5	11.4	87.7	5.0	200
2.0	8.3	120.5	3.9	256
2.5	6.3	158.7	3.1	322.6
3.0	4.6	217.3	2.3	434.8
3.5	3.4	294.1	1.9	526.3
4.0	2.2	454.5	1.3	769.2
4.4	1.73	578.0	1.1	909.0

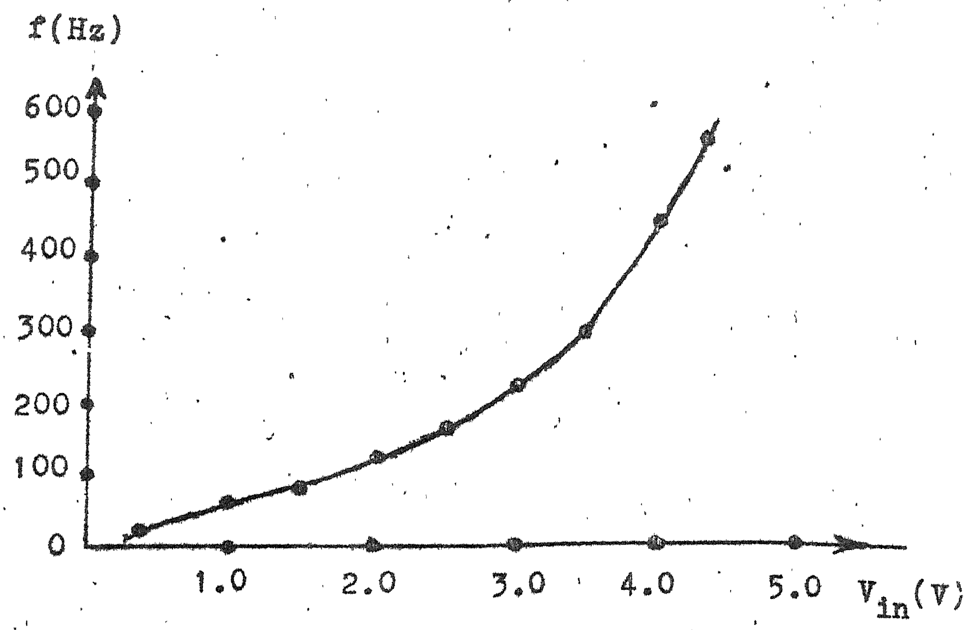


Fig. 8.2 f vs V_i plot for S1

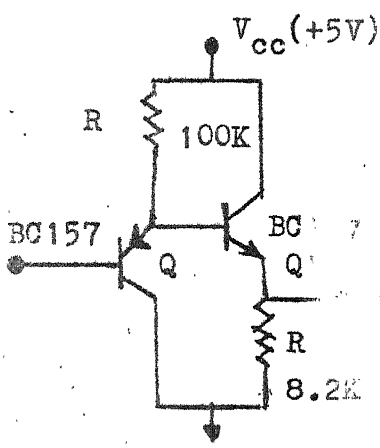


Fig. 8.3 Presso-receptor(R6)

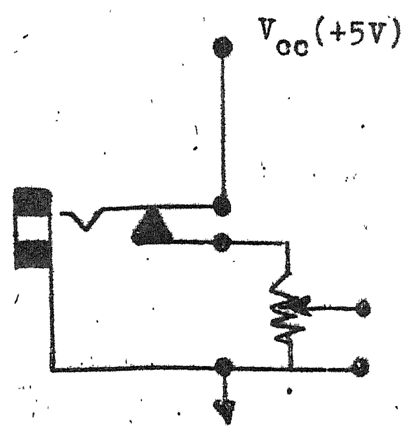


Fig. 8.4 Jack and potentio-meter arrangement

The circuit for the synapse in the spinal reflex is the same as that for receptor in fig. 3.6 with only one excitatory input and no adaptation. The component values are given below

R1 - 22K, R2 - ∞, R3 - 6.8K, R4 - 220K

C1 - 0, C-10 μf Q - BC147

The outputs of the six action potential blocks may be used for providing input to the six input channels of CNS card. The four output channels coming from CNS card are buffered by the hex buffer 74C902 to give a 0-5 V swing. Two outputs may be used for controlling cardiac activity by making the suggested patch card connections. The other two may be connected to muscle cell blocks (circuit shown in fig. 7.3).

A reservoir of oxygen and other vital chemicals is simulated as shown in fig. 6.4. The output of R5 gives the level of reserves. The variable resistance simulating the physical exertion is available on the panel. R6, as shown in fig. 8.3 is a buffer for sensing the pressure in the circulation system.

8.3 Operations and Experiments

The system offers the possibility of carrying out a variety of experiments and investigations. For the convenience in carrying out these experiments, a description of the various

labeled pins on the panel is being given below

GP 1 - GP6 -	Graded generator potentials from receptors R1 - R6. They may be used as inputs to action potential blocks.
GP	Graded voltage signal variable by a potentiometer. This may be used as input for studying the adjustable parameter action potential block (S).
AP, AP1-6	Pulse outputs from the action potential blocks S, S1-S6. They may be used as inputs to CNS.
AP 7	Pulse output on the spinal reflex motoneuron. It may be applied to the skelectal muscle blocks.
AP 8	Pulse output on the output channel M1 of CNS.
AP 9	Pulse output on the output channel M2 of CNS.
AP 10	Pulse output on the output channel C1 of CNS.
AP 11	Pulse output on the output channel C2 of CNS.
AP 12	SA node output
AP 13	AV node output after the common His bundle.
AP 14	Action potential developed in the muscles of the right ventricle.
AP 15	Action potential developed in the muscles of the left ventricle.
MF 1	Force developed in skeletal muscle SM1.
MF 2	Force developed in skeletal muscle SM2.

MF 3	Force developed in the muscles of right atrium (RAM).
MF 4	Force developed in the muscles of right ventricle (RVM).
MF 5	Force developed in the muscles of left atrium (LAM).
MF 6	Force developed in the muscles of left ventricle (LVM).
BP 1	Blood pressure in the right atrium.
BP 2	Blood pressure in the right ventricle.
BP 3	Blood pressure in the lunges.
BP 4	Blood pressure in the left atrium.
BP 5	Blood pressure in the left ventricle.
BP 6	Blood pressure in the aorta.
BP 7 - BP11	Blood pressures in the downstream systemic circulation.

The cardiovascular system can be studied separately by leaving the patch chord connections to the excitatory and inhibitory control inputs of the SA node open. Now the system works under the control of its own automatism. A delay in the conduction of excitation from SA node to ventricles may be observed. For simulating an SA block, the conduction path from the SA node to the AV node has to be left open. Now both the

atria and the ventricles work at the AV node frequency. As the delays from the atria to the ventricles are nearly the same, there is no delay between the contractions of atria and ventricles. For simulating an AV block the conduction path between the AV node and the ventricles are to be removed. A conduction disorder corresponding to the block in the common His bundle branch (section Q in fig. 5.3) may be simulated by connecting the inputs to the ventricles together. In this case, the two ventricles contract in synchronism, but unrelated to the atria. His bundle branch block may be simulated by breaking the conduction path from AV node to one or both the ventricles. The ventricle not receiving the pulses through the AV node runs on its own at a relatively low frequency. Thus the conduction system simulation may be used for showing the various pacemaker levels and complete blocks of different kinds. However as the impairment in the conduction path is being achieved by breaking the path, partial blocks can not be simulated. The effect of external pacemakers may be studied by introducing pulses (TTL levels) from an external pulse generator in the conduction path.

Effects of controls from CNS on the SA node frequency may be studied by introducing pulses at the excitatory and inhibitory inputs of the SA node. These may be derived either

from two outputs of CNS or from external sources.

Results of measurements on the conduction system is given below

SA node

(i) Frequency with both control inputs open 72 bpm.

(ii) Freque cy with excitatory input of 500 Hz (pulsewidth-0.5 ms, 0-5V swing) and inhibitory input open - 90 bpm.

(iii) Frequency with inhibitory input of 500 Hz pulse width - 0.5 ms, 0-5V swing) and excitatory input open - 66 bpm.

AV node

Free running frequency - 53 bpm.

Left ventricle oscillator

Free running frequency - 41

Right ventricle oscillator

Free running frequency - 36

Upper limit of frequency of excitations in the conduction system - 110 bpm.

Delay from the SA node to the ventricles 100 ms

However, the oscillator frequencies may be varied over a wide range by changing the settings of preset potentiometers providing the bias to them.

Pulse widths ~ 100 ms.

A failure in the mechanical contractions of any of the ventricles may be simulated by breaking the connection between that ventricular oscillator and the corresponding muscle.

Effects of transfusion an bleeding on the circulation system may be studied by injecting in or leaking out charge from the circulation system. For this purpose two free potentiometers provided on the left side of the panel may be used. Effects of physical exertion on oxygen and vital chemical reserves may be simulated by the potentiometer on the top as indicated on the panel.

The inputs to the sensory neurons may be provided by the potentiometers on the left side. There is the provision of providing external signals through the jack inputs as shown in fig. 8.4. These signals may be derived from some appropriate transducers. However, they should be in 0-5V range. The potentiometer may be used to control the magnitude of the signal. In case, one is not interested in the generator potential block, the signals from the potentiometer may be directly given to the action potential blocks. The efferent outputs from the CNS may be given to the skeletal muscles shown on the panel and the SA node controls. Alternatively, they may be used for driving external actuators with the help of appropriate interfacing.

CNS card is available on the panel through input and output channels only. However, there is complete flexibility as regards the choice of connections. A possible set of connections is suggested on the panel. Various kinds of conditioned reflexes, learning processes and autonomic control activities may be simulated by appropriate software stored in the ROM on the CNS card.

In writing the program, one has to consider the following factors -

(a) Cycle time (T) - The time interval at which the processor is interrupted. Execution time for the program must be within cycle time.

(b) Input frequency (f_i) - Each input port is read at the start of a new cycle time. The count N_i accumulated in the counter is given as

$$N_i = f_i \quad T \tag{8.1}$$

To avoid a possible overflow, N_i must be less than 256.

(c) Output frequency (f_o) - The data to each output port is refreshed once in each cycle time. The 8-bit PRM in the output port is a BCD one and hence appropriate conversion should be done if the results after the processing are in the binary form. The timer output from 8156 serves as the

clock input to the PRMs. This is divided by 100 to provide the interrupt on RST 7.5 line of 8085. Thus the frequency of the PRM clock is given as

$$f_{PRM} = \frac{100}{T} \qquad (8.2)$$

If the data latched on the PRM input be No (BCD) then the output frequency is given as

$$f_o = \frac{No}{T} \qquad (8.3)$$

8.4 A Program for Testing the Hardware of CNS Card

Listing of a program for testing the hardware of CNS card is given in the appendix (TST). It follows the program structure suggested in section 7.1.5.

For a cycle time of 100 msec, the timer output frequency should be 1 KHz which requires a division by 2500 of the system clock (2.5 MHz). A flow chart description of the program is given in fig. 8.5. Trap is kept low. After application of a RESET pulse, a frequency of 1 KHz from the timer indicates that the organisation of 8085, 8156 and 2716 is all right. A proper matching of input port and output port frequencies means that the entire hardware organisation of the card is in order.

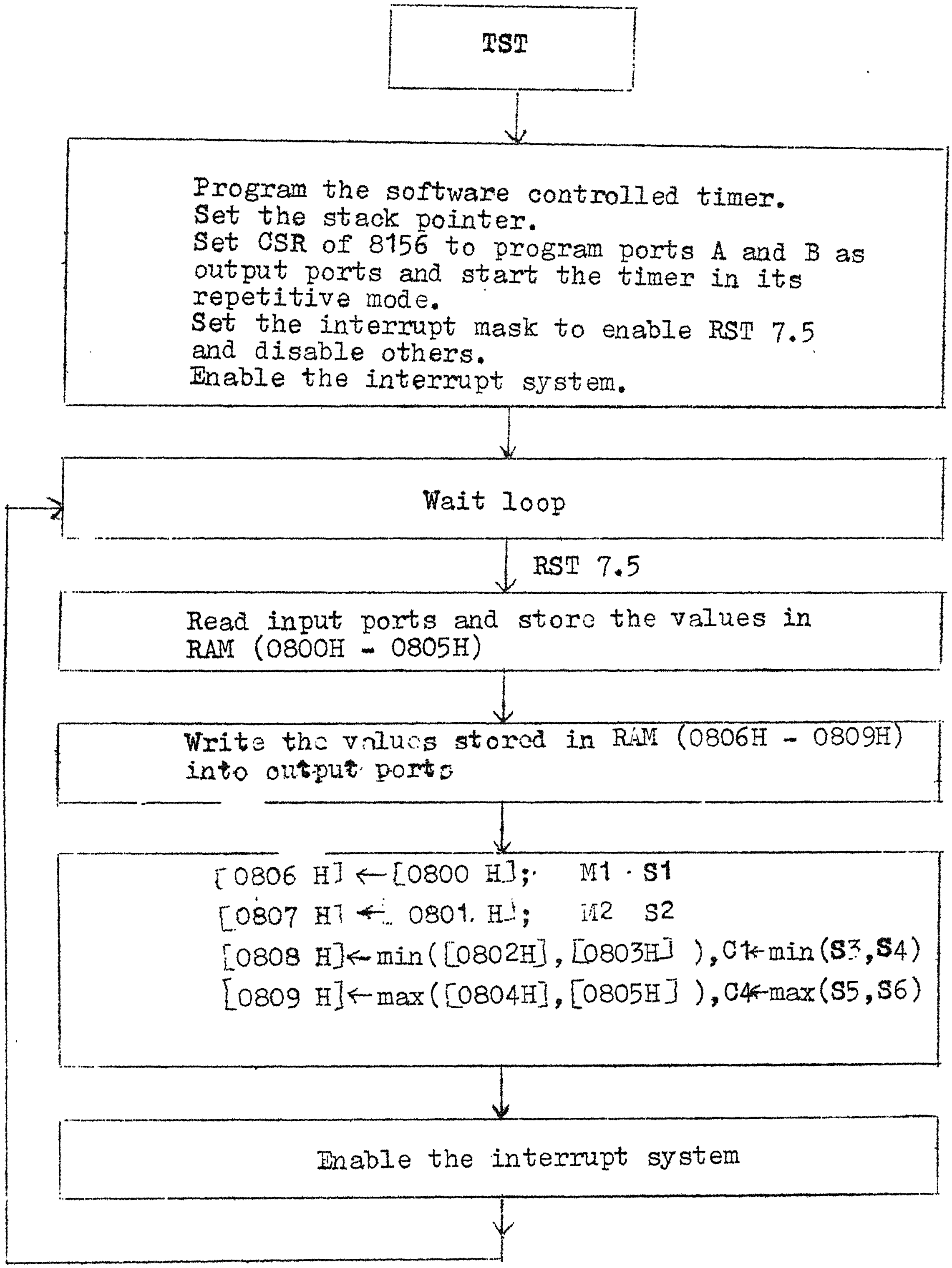


Fig. 8.5 Flow diagram for testing program (TST)

8.5 A Program Simulating Simple Conditioned Reflexes and Autonomic Control of SA node

In modelling a simple conditioned reflex (fully deterministic behaviour), we take the case of a response R to a direct stimulus S_d and an associative stimulus S_a. C is a coefficient of association between S_d and S_a and is refreshed in each cycle according to the relation

$$C_{i+1} = C_i + \Delta C_i \qquad (8.4)$$

where ΔC_i is a quantity depending on the stimuli as shown in fig. 8.6(a). The response R is determined by S_d, S_a and C as in the manner shown in fig. 8.6(b).

In present studies, S1, S2 and C1 have been taken as S_d, S_a and R. $T_{sd} = T_{sa} = T_s$. The conditioned reflex is modelled by the simple algorithm presented in fig. 8.6(c).

Another conditioned reflex is modelled with S4 as the direct stimulus, S2 and S3 as indirect stimuli and M2 as the response. The manner in which C is transformed, the response and the algorithm for simulating this reflex are shown in fig. 8.7.

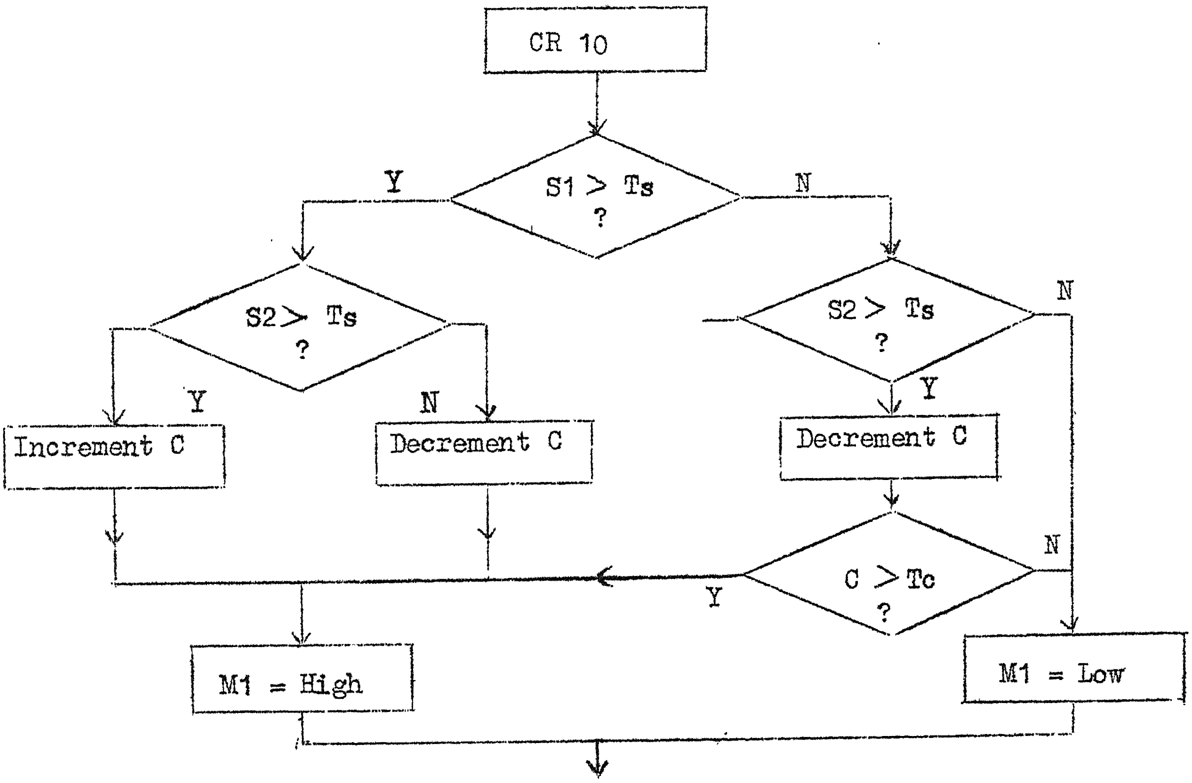
For the autonomic control, oxygen level is sensed through R_5 and S_5. Pressure is sensed through R_6 and S_6. C_1 and C_2 are

S2 \ S1	S1 ≤ Ts	S1 > Ts
S2 ≤ Ts	0	-K
S2 > Ts	- K	+K

(a) Dependence of $\triangle C$ on S1 and S2

C \ S1,S2	S1 ≤ Ts S2 ≤ Ts	S1 ≤ Ts S2 > Ts	S1 > Ts S2 > Ts	S1 > Ts S2 ≤ Ts
C ≤ Tc	L	L	H	H
C > Tc	L	H	H	H

(b) Dependence of M1 on S1, S2 and C



(c) Algorithm

Fig. 8.6 Conditioned reflex involving S1,S2 and M1

S4 \ S2, S3	$S2 \leq Ts$, $S3 \leq Ts$	$S2 \leq Ts$, $S3 > Ts$	$S2 > Ts$, $S3 > Ts$	$S2 > Ts$, $S3 \leq Ts$
$S4 \leq Ts$	0	0	− K	0
$S4 > Ts$	− K	0	+ K	0

(a) Dependence of C* on S2, S3, S4

S4, C \ S2, S3	$S2 \leq Ts$, $S3 \leq Ts$	$S2 \leq Ts$, $S3 > Ts$	$S2 > Ts$, $S3 > Ts$	$S2 > Ts$, $S3 \leq Ts$
$S4 \leq Ts$, $C \leq Tc$	L	L	L	L
$S4 \leq Ts$, $C > Tc$	L	L	H	L
$S4 > Ts$, $C > Tc$	H	H	H	H
$S4 > Ts$, $C \leq Tc$	H	H	H	H

(b) Dependence of M2 on S2, S3, S4 and C

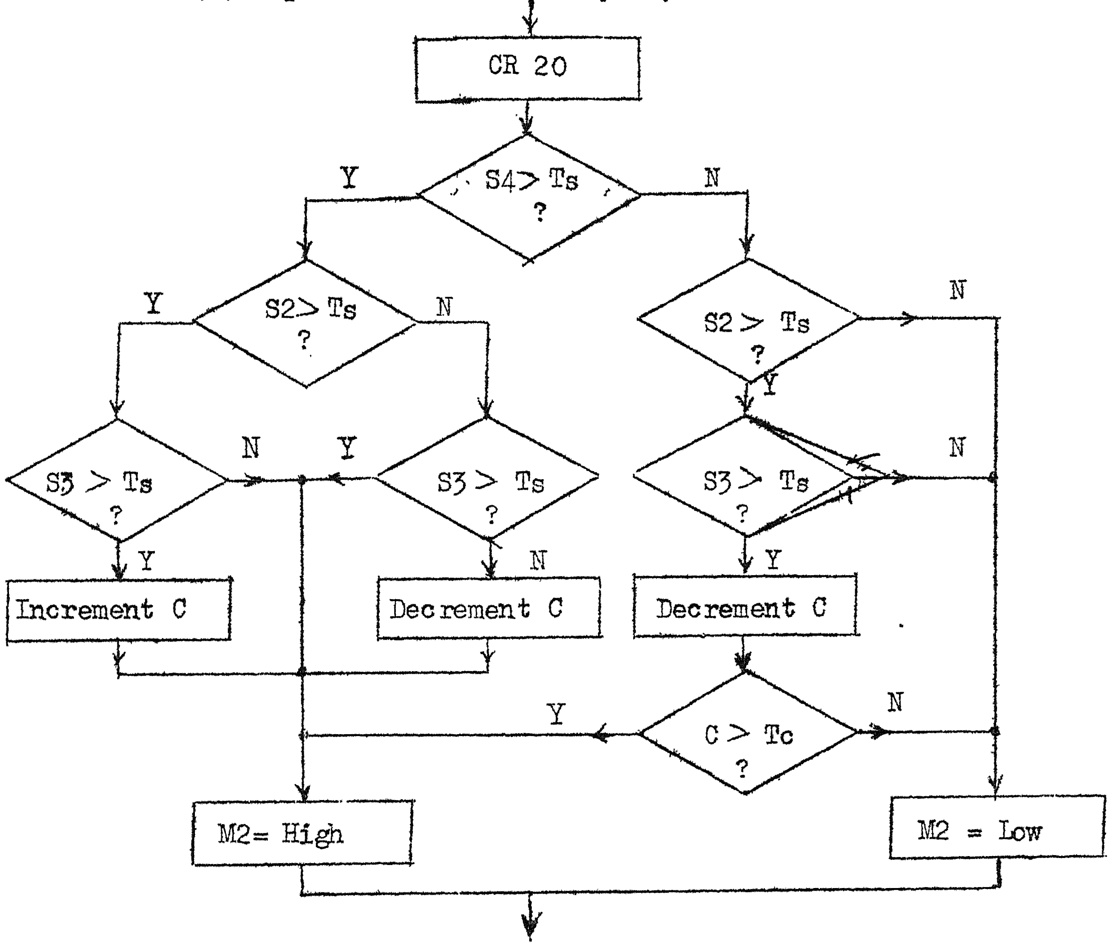
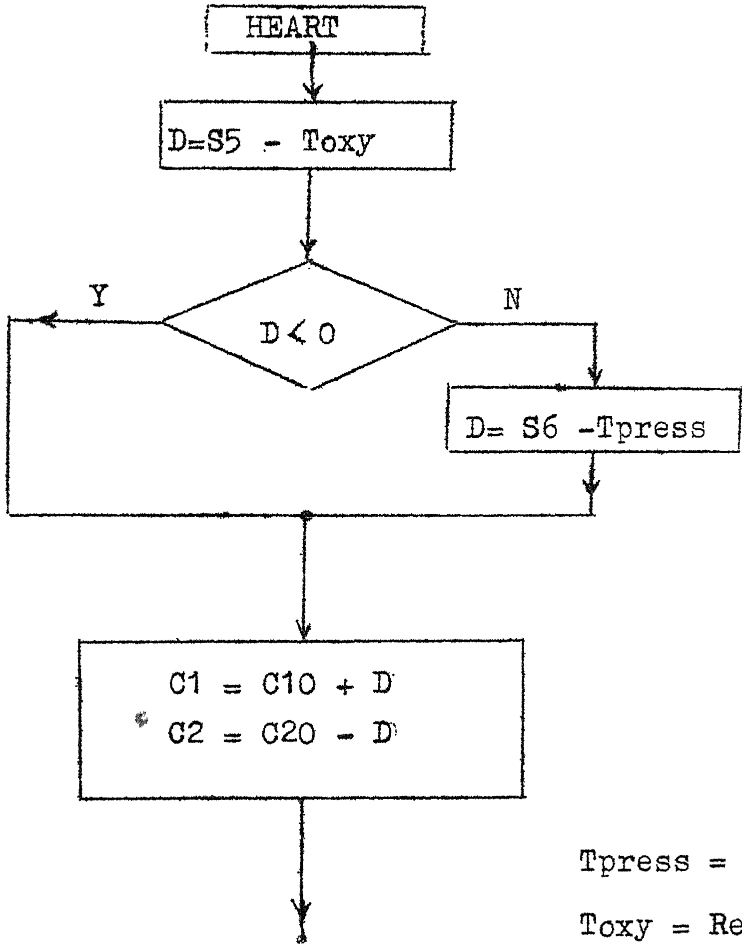


Fig. 8.7 Conditioned reflex involving S2, S3, S4 and M2

* This is different from 'C' in fig. 8.6



Tpress = Reference for pressure
Toxy = Reference for oxygen level
C10 = Tone value of C1
C20 = Tone value of C2

Fig. 8.7 Algorithm for autonomic control of SA node frequency

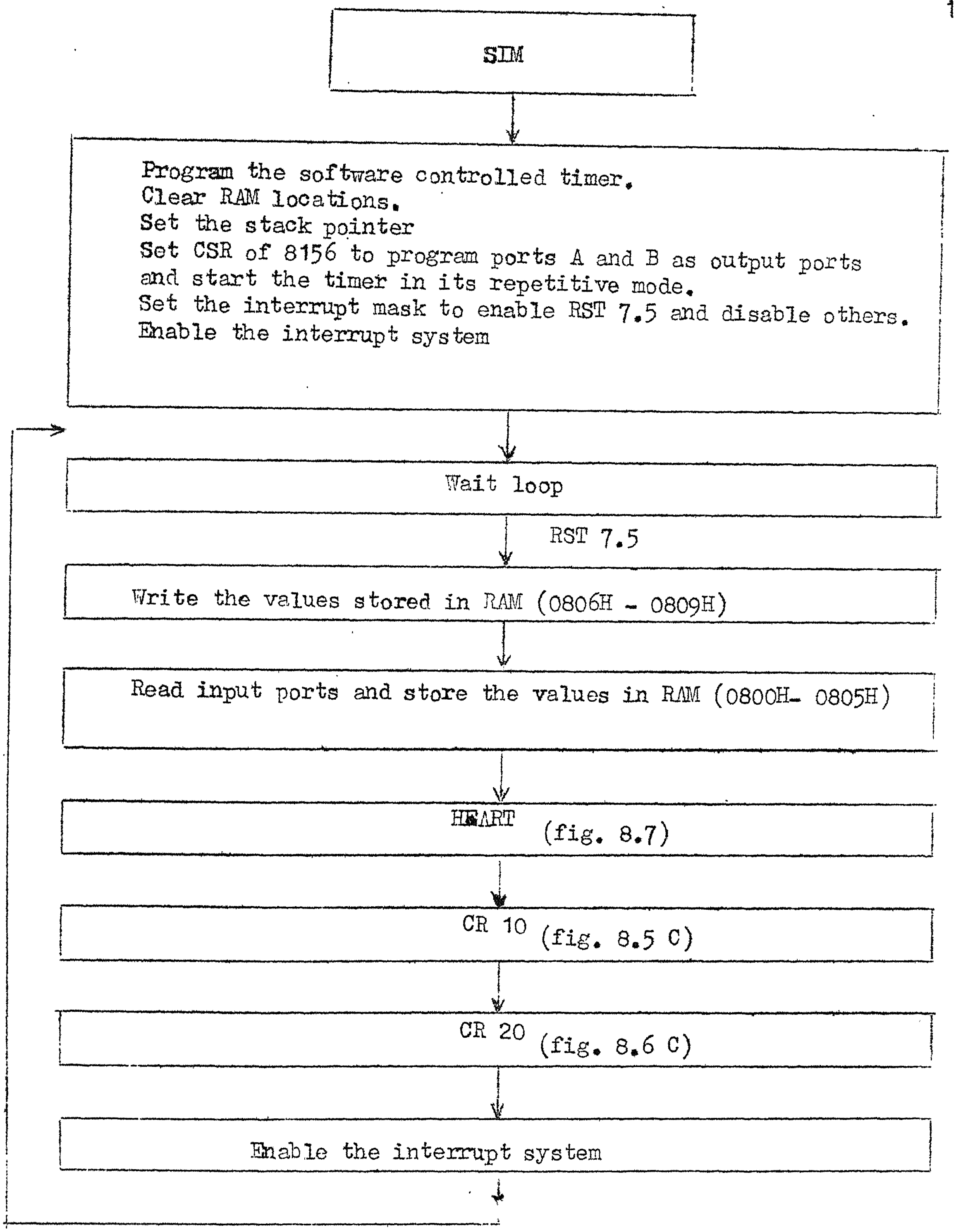


Fig. 8.9 Flow diagram of the program SIM

A RESET pulse (by pressing RESTART on the panel) clears all the past experience and the system starts learning afresh.

8.6 Suggestions for Experiments and Further Work

The system developed offers flexibility for simulating a variety of structures and behaviours. By coupling transducer signals at the input to the nervous system and replacing muscle simulation circuits by appropriate actuators, a realistic simulation for many activities of living organisms may be developed.

In the simulation of simple conditioned reflexes described in the previous section, the duration of 'learning' and 'forgetting' may be increased by using multi byte word to represent C. As only a small fraction of the cycle time is used for the execution of program simulating conditioned reflexes, one may write software for simulating much more involved learning processes with multiple loops of conditioned and unconditioned reflexes-making use of full cycle time.

It is possible to use the input potentiometers (or whatever signal sources are being used) to provide certain parameters to the program. One possible way is making use of the TRAP. When TRAP is pressed, the program records the various input port readings and interprets them to give these

parameters. In an alternative approach,the input readings in the cycles just after the application of RESET pulse may be used to define these parameters. After defining these parameters, the inputs values are accepted as stimuli. By using these techniques, certain degree of flexibility in the program is achieved as one can vary the parameters like learning speeds, stimulus thresholds etc without changing the program stored in the EPROM.

The work can be further extended in several directions. One may develop more elaborate models for simulating the neurons. In case miniaturisation of the circuit be possible, these models may be used for networks simulating reflexes and possibly many involved processes in CNS. The simulation of the cardiovascular system suggests many possibilities for developing much more elaborate simulations. In place of treating pacemakers as localised oscillators, a simulation for distributed activity of each pacemaker may be simulated. Then the partial blocks in the conduction system and fibrillation etc also can be simulated. The circulation system simulation may be made more realistic by using a large no. of muscle elements in the musculature of heart chambers and thus simulating a propagation of contraction wave and making the circulation system much more distributed. Furthermore, linear resistances in the circulation

path may be replaced by nonlinear resistances simulating the constriction and dilation in blood vessels.

By choosing a faster processor in the CNS simulation the no. of input and output channels can be increased enabling the simulatinn of more realistic processes. By introducing a random quantity statistically defined in a certain way in addition to C in relation (8.4) for transforming C, random processes in the reflexes may be simulated.

REFERENCES

Chapter II

1. Ruch, T.C and Patton, H.D. (eds.), "Physiology and Biophysics" (Ch II pp 26-53), W.B. Saunders Co, Philadelphia, 1965.

2. Plonsey, R. & Fleming, D.G.,"Bioelectric Phenomena" (Ch.IV) McGraw Hill Book Co. - New York, 1969.

3. Gawronski, R (ed), "Bionics -The nervous system as a control system", (Ch. I, pp), Polish Scientific Publishers-Warszawa, 1971.

4. Plonsey, R & Fleming D.G.,"Bioelectric Phenomena" (Ch I,pp. 9-12), McGraw Hill Book Co. New York, 1969.

5. Plonsey, R & Fleming D.G., "Bioelectric Phenomena" (Ch I, pp. 18-21), McGraw Hill Book Co. New York, 1969.

6. Babsky, E.B.,Khodorov,B.I.,Kositsky G.I. & Zubkov,A.A, " Human Physiology" Vd II (Ch XIV), Mir Publishers,Moscow, 1977.

7. Gawronski, R, "Bionics - The nervous system as a control system", (Ch III, pp), Polish Scientific Publishers - Warszawa, 1971.

Chapter III

1. Gawronski,R (ed), "Bionics - The nervous system as a control system", (Ch II, pp 32-33), Polish Scientific Publishers, Warszawa, 1971.

2. Gawronski,(ed) R, "Bionics - The nervous system as a control system", (Ch II, pp 48-50), Polish Scientific Publishers, Warszawa, 1971.

3. Crane D.C.,"Neuristor - A novel device and system concept", Proc. 1RE vol. 50, pp.2048 -2060, Oct. 1962.

4. Cote, A.J.,"A neuristor prototype", Proc. 1RE vol. 49, pp 1430 - 31, Sept. 1961.

5. Nagumo, J et al,"An active pulse transmission line simulating nerve axon", Proc. 1RE, vol. 50, pp 2061-2070, Oct. 1962.

6. Mattson,R.H.,"A neuristor realisation",Proc. 1RE,vol. 52, pp 618-619, May 1964.

7. Plonsey, R & Fleming, D.G.,"Bioelectric Phenomena" (ChIV), McGraw Hill Book Co.,New York 1969.

8. Lewis E.R.,"Using Electronic circuits to model simple neuroelectric interactions", Proc. IEEE, vol. 56, pp 931-949, June 1968.

9. Johnson,R.N. & Hanna,G.R.,"Membrane Model a single transistor analog of excitable membrane", J.thear Biol,vol. 22, pp. 401-411, March 1969.

10. Roy,G.,"A simple electronic analog of the squid axon membrane :the NEOROPET" IEEE trans. B.omed Eng., vol.IME-19 pp. 60-63, Jan 1972.

11. Pottala,E.W. et al,"A dendntic compartment model neuron", IEEE Trans, Biomed, Engg. vol. BME-20, pp 132-139, Mar 1973.

12. Brockman, "A simple electronic neuron model indorporating both active and passive responses", EE Trans. Biomed Engg. vol. BME-26, Nov. 1979.

13. Gawronski, R(ed),"Bionics -- The nervous system as a control system", (Ch II, pp. 50-93), Polish Scientific Publishers-Warszawa 1971.

14. French, A.S. and Stein, R.B.,"A flexible neural analog using integrated circuits", IEEE Trans Biomed Engg; vol. BME-15,pp 138-151 July 1968.

15. Thexton, "A modification of the French Stein neural analog" IEEE Trans. Biomed Engg, vol. BME-21, pp 339-341,July 1974.

16. Saxena et al, "An electronic model of neuron",Journal of IE (India) vol. 58-ET2, Dec 1977.

Chapter IV

1. Vander,A.J.,Sherman,J.H. & Luuano,D.S., "Human Physiology" (Ch II, pp 162-171), Tata McGraw-Hill Publishing Co. Ltd. New Delhi , 1977

2. Klir,J. & Valach, M, "Cybernetic Modelling", (Ch X,pp 234-235),Iliffe Books Ltd.,London 1967.

3. Basky,E.B.,Khodorov,B.I.,Kositsky,G.I. and Zubkov,A.A., "Human Physiology" vol II (Ch XIII), Mir Publishers, March 1977.

4. Klir,J. and Valach,M.,"Cybernetic Modelling", (Ch X, pp. 232-233), Illiffe Book Co.,London,1967.

5. Wyburn,G.M.,"The Nervous System" (Ch II),Academic Press, London & New York, 1960.

6. Wyburn, G.M.,"The Nervous System" (Ch X),Academic Press, London & New York, 1960.

7. Singh,J.,"Information Theory, Language and Cybernetics", (Ch X), Dover Publications, Inc. New York, 1966.

8. Ruch, T.C. and Patton, H.D.(ed),"Physiology and Biophysics", (Ch XXIV), W.B. Sounders Co, Philadelphia, 1965.

9. Babsky,E.B, Khodorov,B.I.,Kositsky,G.I. and Zubkov,A.A. "Human Physiology" Vol II (Ch XVII), Mir Publishers- Moscow 1977.

Chapter V

1. Gawronski,R. (ed),"Bionics - The nervous system as a control system", (pp 171).

2. Babsky,E.B.,Khodorov,B.I., Kositsky,G.I. & Zubkov,A.A., "Human Physiology",vol I (Ch IV, p87), Mir Publishers, Moscow, 1977.

3. Plonsey,R. & Fleming D.G.,"Bioelectric Phenomena",

4. Babsky,E.B, Khodorov,B.I.,Kositsky, G.I. & Zubkov, A.A., "Human Physiology", vol I (Ch IV, p 89-91), Mir Publishers, Moscow, 1977.

5. Babsky, E.B., Khodorov, B.I., Kositsky, G.I. & Zubkov, A.A. "Human Physiology", vol. I (Ch IV, p 103-105), Mir Publishers, Moscow, 1977 .

6. Kishan, N., "A cardiac monitor/stimulator system", M.Tech Thesis, IIT-Kanpur, July 1979.

7. Cromwell, L., Fred, J.W., Erich, A.P. &Leo, B.U., "Biomedical Instrumentation & measurements" (Ch 5, pp 65-66), Prentice-Hall Inc. New Jersey, 1973.

8. Babsky, E.G. Khodorov, B.I., Kositsky, G.I. & Zubkov, A.A., "Human Physiology", vol 1 (Ch IV, pp 110), Mir Publishers, Moscow, 1977.

9. Babsky, E.G., Khodorov, B.I., Kositsky, G.I. & Zubkov, A.A., "Human Physiology", vol 1 (Ch IV, pp 145-146), Mir Publishers, Moscow, 1977.

10. Babsky, E.G., Khodorov, B.I., Kositsky, G.I. & Zubkov, A.A., "Human Physiology", vol.1 (Ch III, pp 82-83), Mir Publishers, Moscow, 1977.

11. Wybusn, G.M., "The Nervous System", (Ch X, pp 135-137), Academic Press- London & New York, 1960.

12. Babsky, E.G., Khodorov, B.I., Kositsky, G.I. & Zubkov, A.A., "Human Physiology", vol.1 (Ch IV, pp 126-130).

APPENDIX

A. Linear Applications of CMOS Inverter

The input-output characteristic of a CMOS inverter gate with $V_{CC} = 5V$ is shown in fig. A.1 . It has a very ~~high gain at $V_i = V_t$ and a high input~~ impedance. It can be looked upon as an Op Amp with the +ve input internally returned to V_t and the -ve input being accessible from outside. This gate can be used as an Op Amp for many applications except of course as a voltage follower, because +ve input is unavailable.

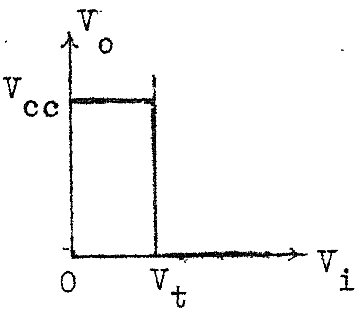


Fig. A.1

Inverting Summer

An inverting summer is shown in fig. A.2 . From KCL at the input

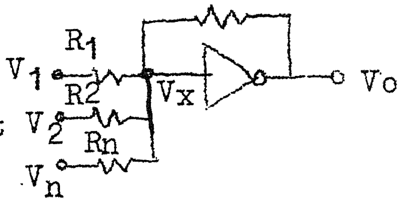


Fig. A.2

$$\sum_i \frac{V_i - V_x}{R_i} + \frac{V_o - V_x}{R_f} = 0$$

Assuming that the inputs are not forcing V_x towards either of the saturation levels, $V_x = V_t$

Hence we have

$$V_o = V_t - \frac{R_f}{R_i} \sum \left(\frac{V_i - V_t}{R_i} \right)$$

For a single input :

$$V_o = V_t - \frac{R_f}{R_i} (V_i - V_t)$$

for two inputs :

$$V_o = V_t - \frac{R_f}{R_i} (V_i - V_t) - \frac{R_f}{R_2} (V_2 - V_t)$$

Comparator

Making use of one unity gain inverting circuit and another gate for summing, a comparator may be realised.

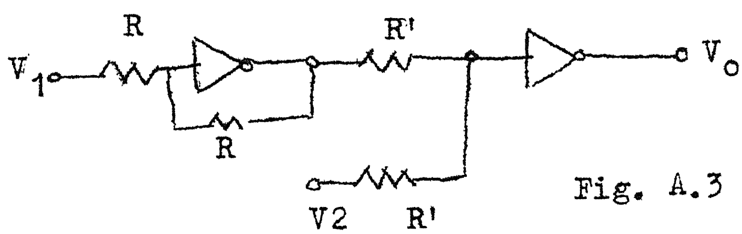


Fig. A.3

$$V_1' = V_t - (V_1 - V_t) = 2 V_t - V_1$$

$$V_x = \frac{V_1' + V_2}{2} = \frac{V_2 - V_1 + 2V_t}{2} = V_t + \frac{V_2 - V_1}{2}$$

$$\text{or} \quad V_x - V_t = \frac{V_2 - V_1}{2}$$

Hence for $V_2 > V_1$; $V_x - V_t > 0 \Rightarrow V_o =$ Low

for $V_2 > V_1$; $V_x - V_t > 0 \Rightarrow V_o =$ High

Thus V_1 is the + input and V_2 is the - input

For increasing the gain and reducing the error range, two more gate may be cascaded. The circuit is shown in fig. A.4

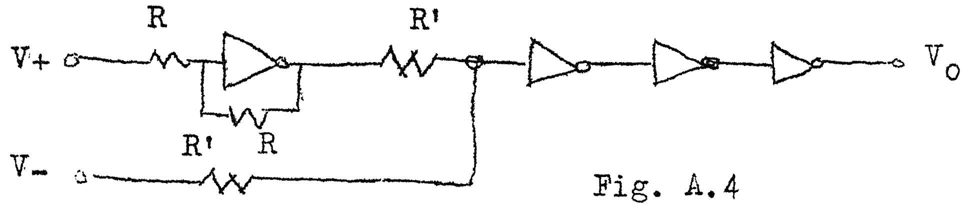


Fig. A.4

Input V_+ must be between $2V_t$ and so that the inverter is in its linear range

Error in the comparator

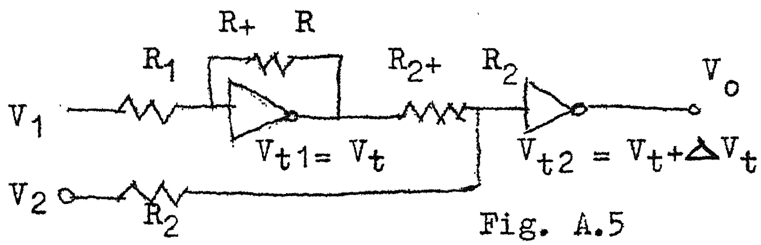


Fig. A.5

Error in the comparator may arise from two sources: tolerance in the resistances and mismatch in the threshold voltage for the gates. Referring to fig. A.5.

$$\frac{V_1 - V_{t1}}{R_1} = \frac{V_{t1} - V_1'}{R_1 + \Delta R_1}$$

$$V' \simeq V_{t1}\left(2 + \frac{\Delta R_1}{R_1}\right) - \left(1 + \frac{\Delta R_1}{R_1}\right) V_1$$

$$V_x = (R_2 V' + (R_2 + \Delta R_2) V_2)/(2R_2 + \Delta R_2)$$

$$\Rightarrow V_x - V_{t2} - \left(1 + \frac{\Delta R_1}{2R_1} - \frac{\Delta R_2}{2R_2}\right) V_{t1} - V_{t2}$$

$$+ \frac{V_2 - V_1}{2} + \frac{V_2 + V_1}{2} \quad \frac{2R_2}{2R_2} - \frac{V_1}{2} \frac{\Delta R_1}{R_1}$$

$$\text{error} = V_{t1} - V_{t2} + \left(\frac{\Delta R_1}{2R_1} - \frac{\Delta R_2}{2R_2}\right) V_{t1}$$

$$+ \frac{V_2 + V_1}{2} \quad \frac{\Delta R_2}{2R_2} - \frac{V_1}{2} \quad \frac{\Delta R_1}{R_1}$$

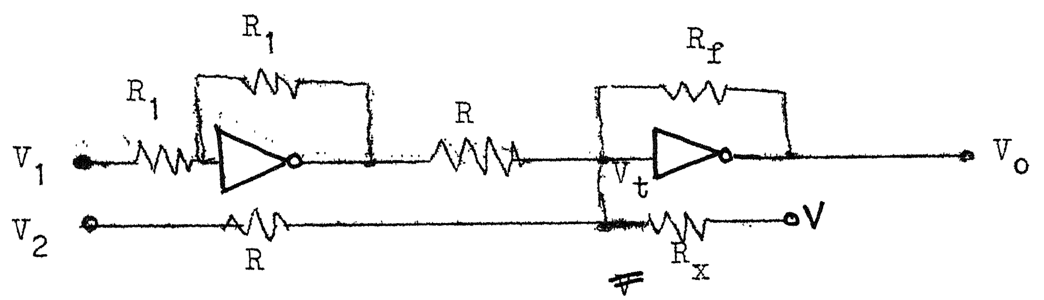
$$\text{Max error} = \Delta V_t + \frac{\Delta R}{R} V_t + \frac{\Delta R}{R} \frac{V_2}{2} + \frac{\Delta R}{R} \frac{V_1}{2}$$

$$= \Delta V_t + \frac{\Delta R}{R} \left(V_t + \frac{V_2}{2} + V_1 \right)$$

Thus error has got two terms, one depending on V_1 & V_2 while other on ΔV_t and V_t.

Differential Amp

A differential amp can be made with two CMOS inverter gates, with one as inverter and other as inverting summer as shown in fig. A.6.



$$V_1' = 2V_t - V_1$$

$$\frac{V_1' - V_t}{R} + \frac{V_2 - V_t}{R} + \frac{V - V_t}{R_x} + \frac{V_o - V_t}{R_f} = 0$$

or $$V_o = V_t - R_f \left(\frac{V - V_t}{R_x} + \frac{V_2 - V_t}{R} + \frac{V_t - V_1}{R} \right)$$

$$= \frac{R_f}{R} (V_1 - V_2) + V_t - \frac{V - V_t}{R_x} R_f$$

If $R_f = R_x$ and $V = 2V_t$

Then

$$V_o = \frac{R_f}{R} (V_1 - V_2)$$

B. PC Card Layouts

The PC card layouts for the three cards in the system are given in fig. PC1-PC3 as the following

PC1 (a) : CNS card (component side)

PC1 (b) : CNS card (back)

PC2 (a) : Cardiovascular system card (component side)

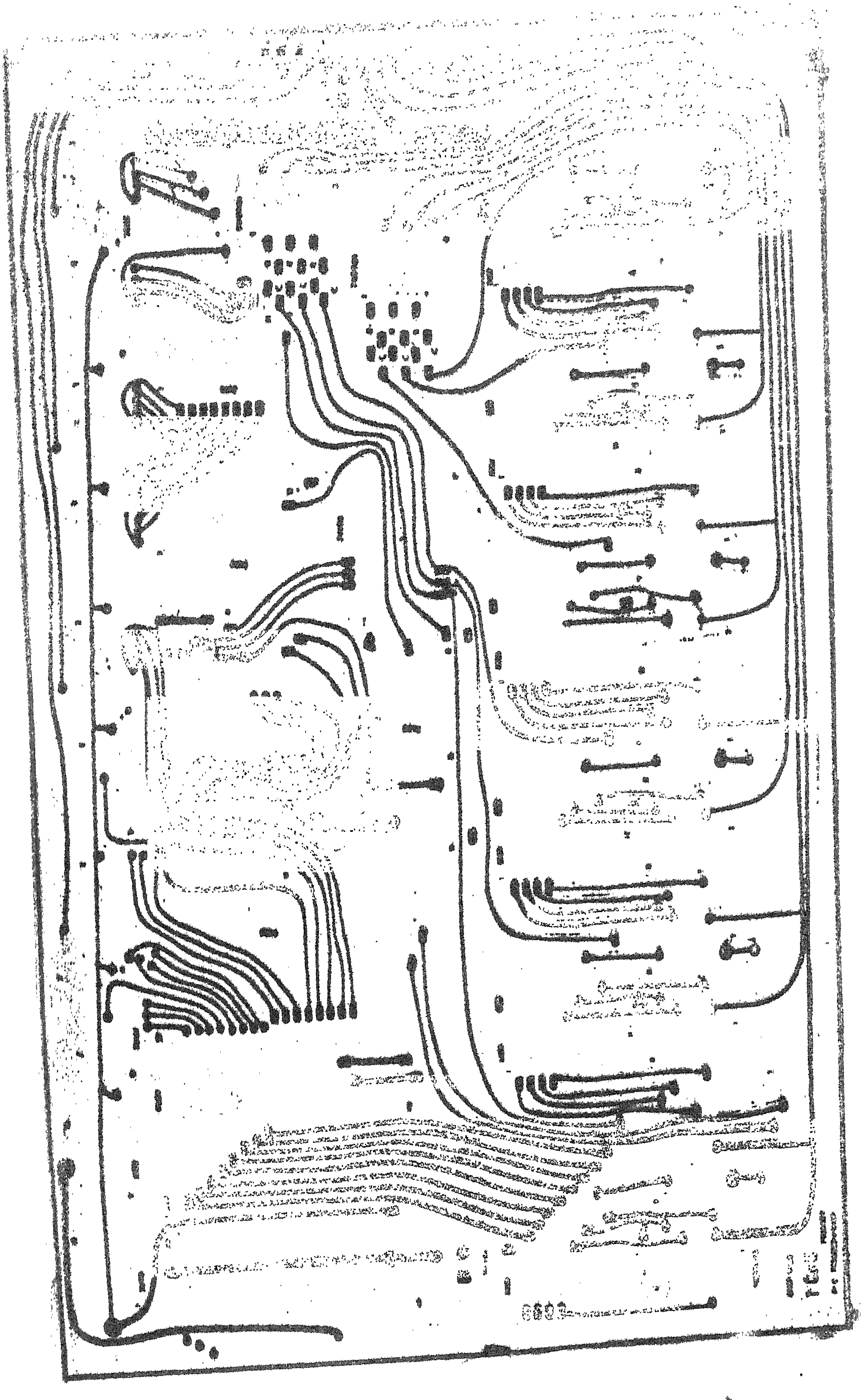
PC2 (b) : Cardiovascular system card (back)

PC3 (a) : PNS card (component side)

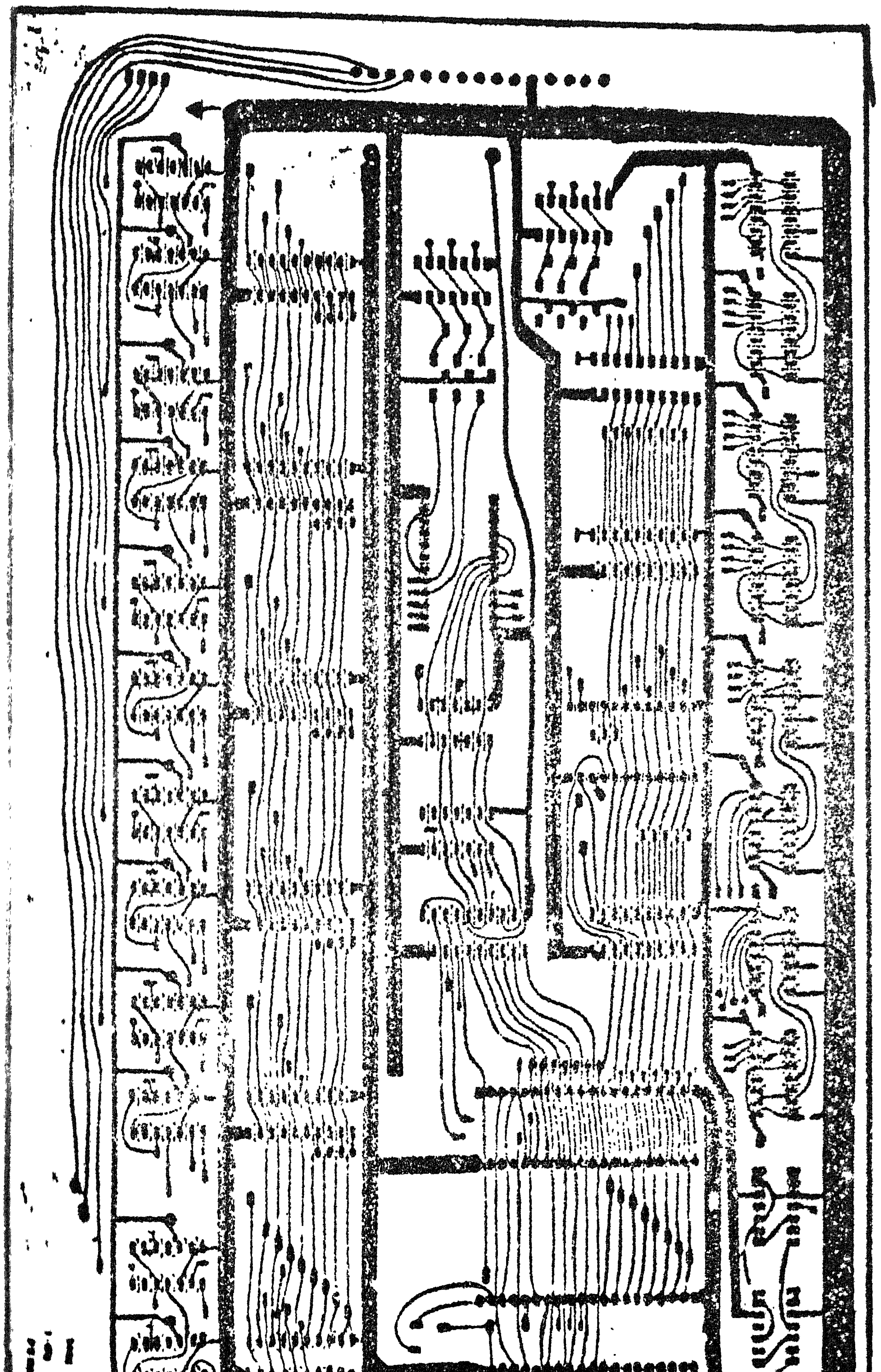
PC3 (b) : PNS card (back)

C. Program Listings

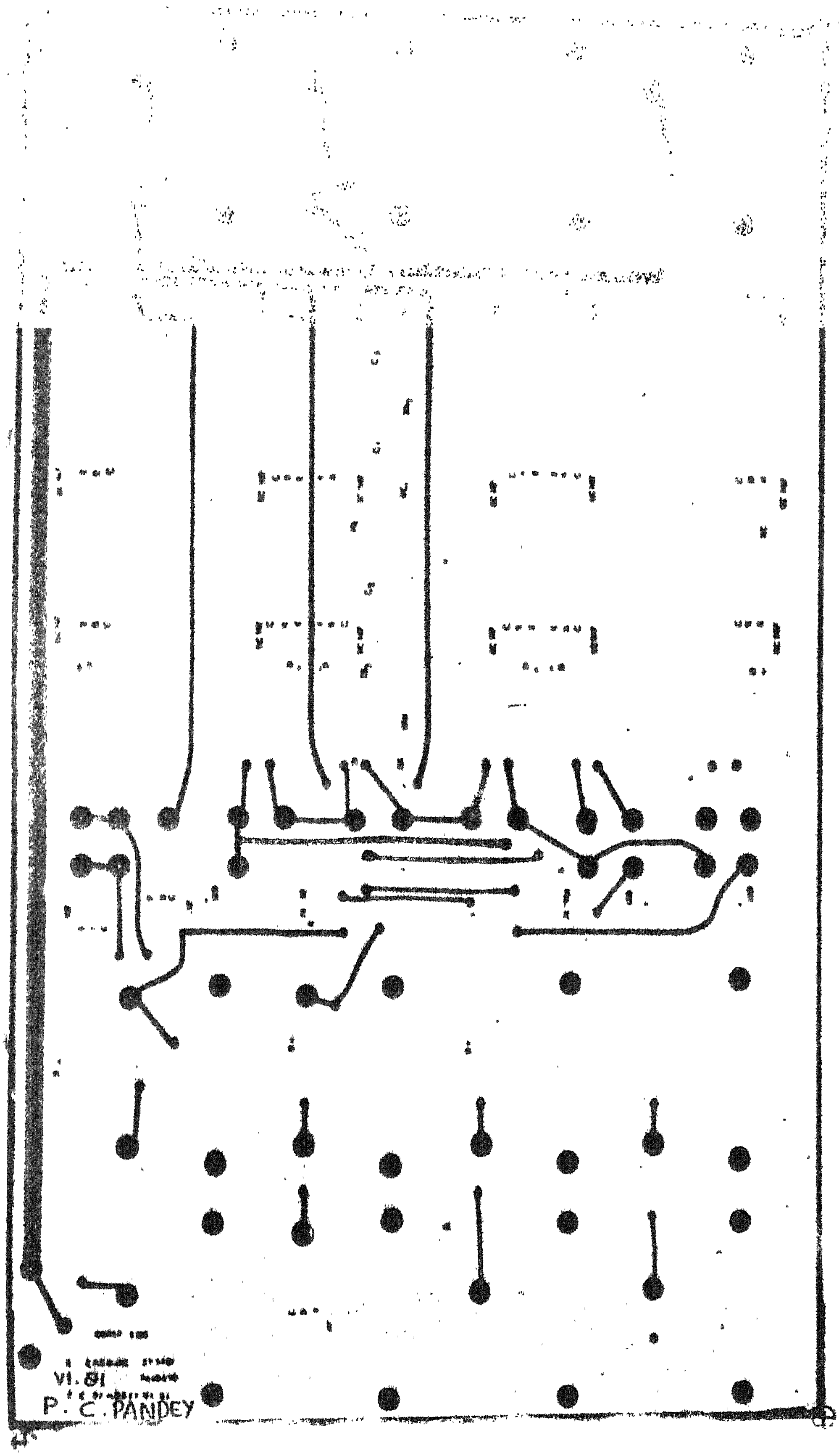
Listing of the two programs TST and SIM are enclosed.



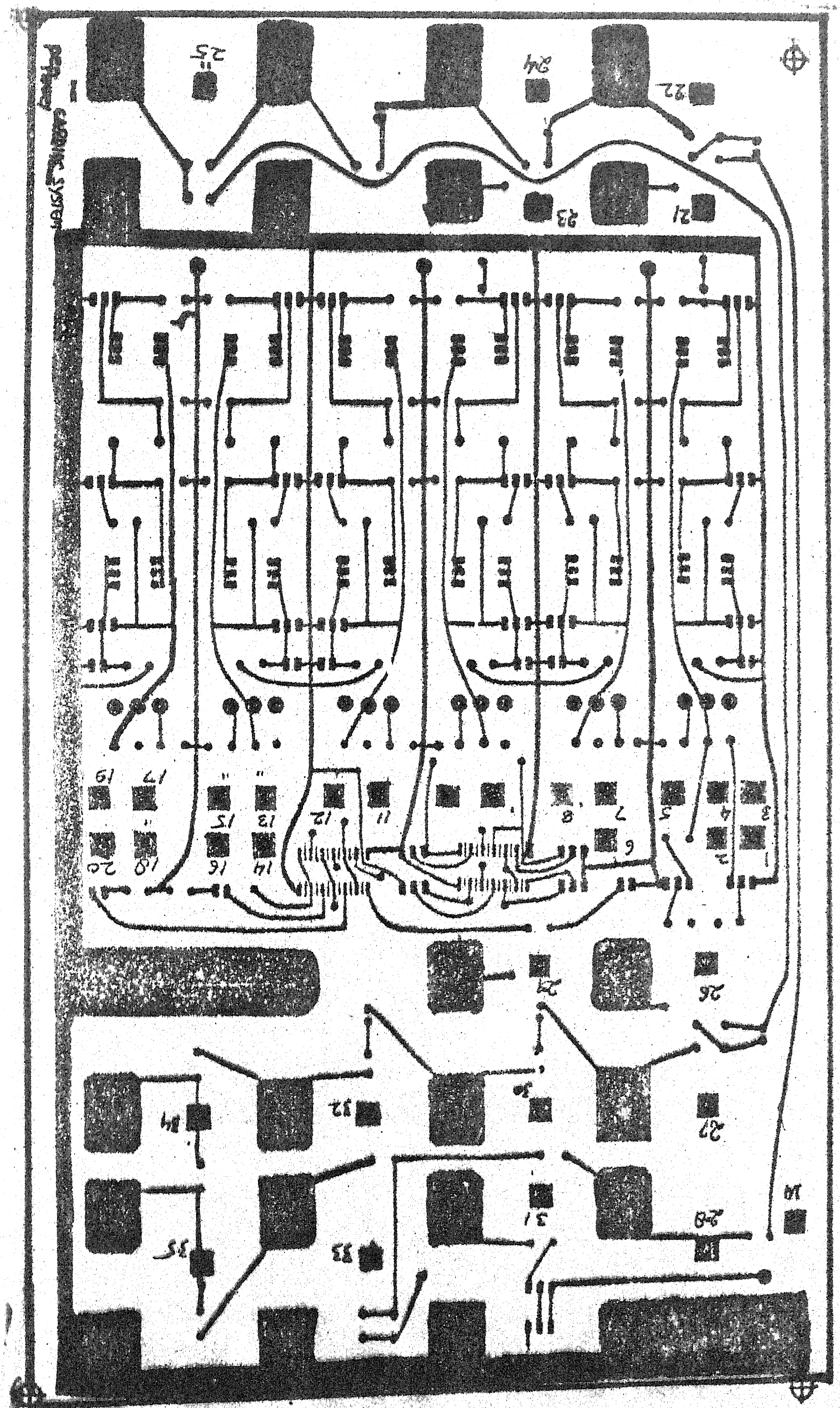
PC 1(a) Central Nervous System Card (component side)



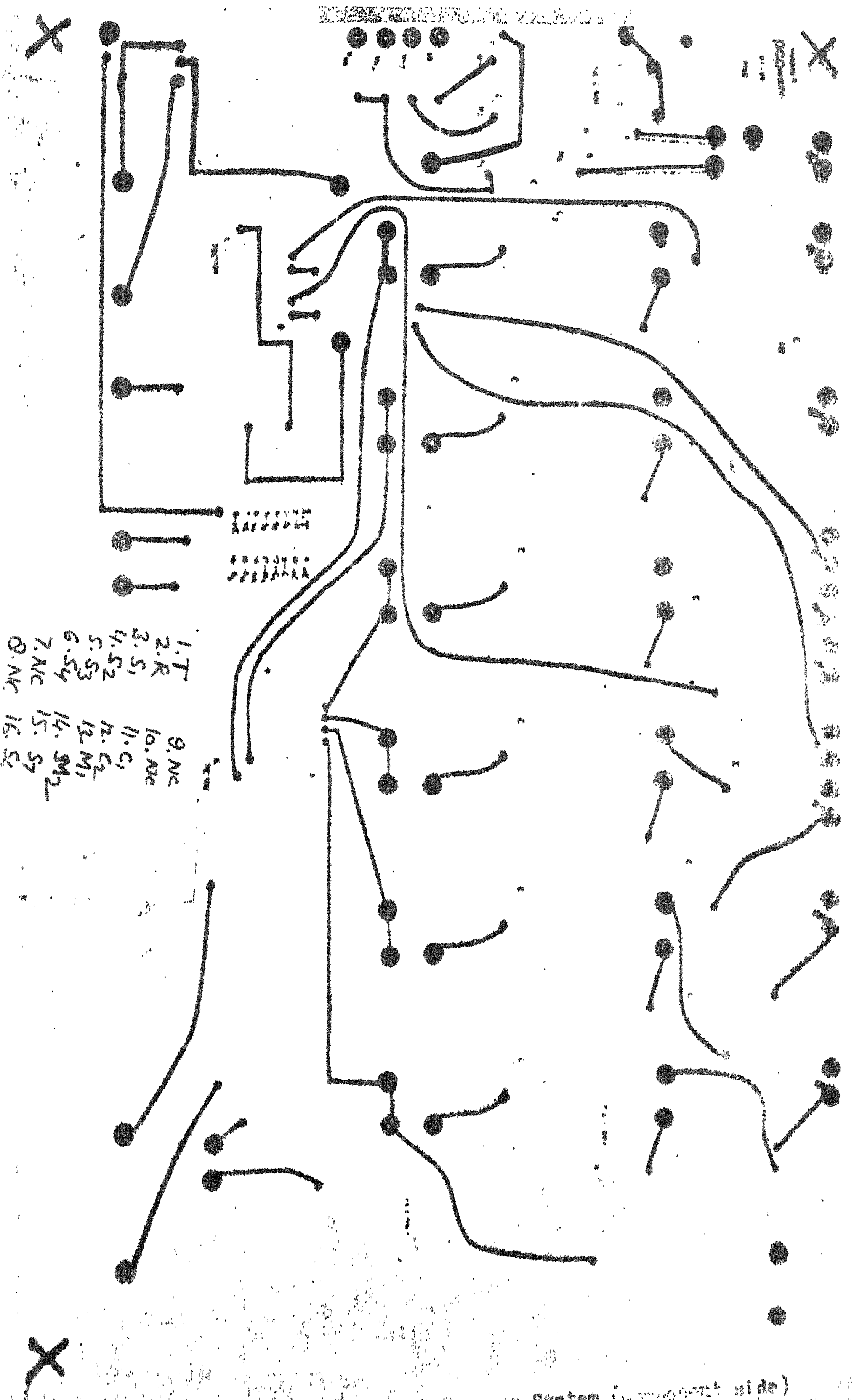
PC 1 (b). Central Nervous System Card (back)



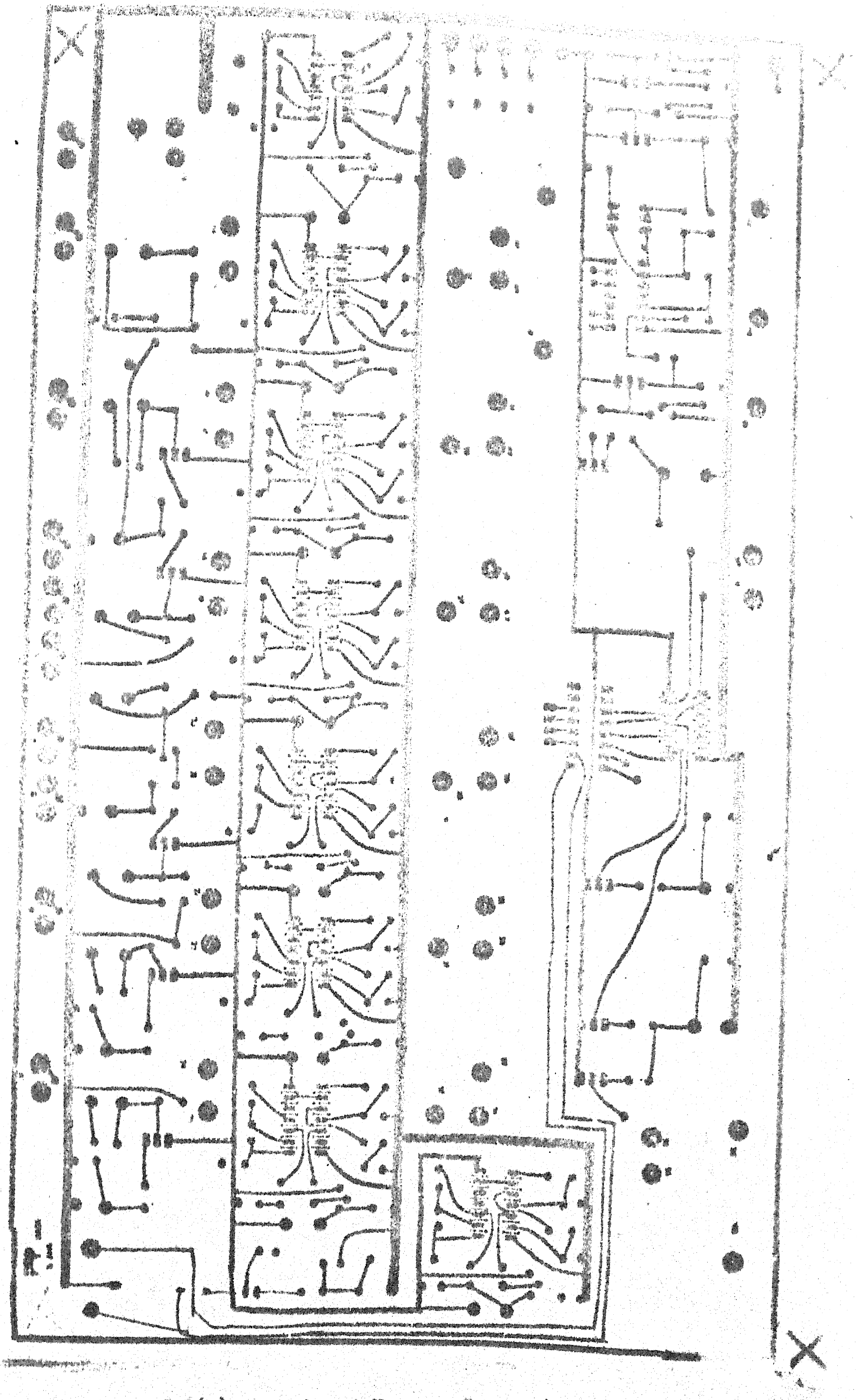
2(a) Cardiovascul System Card (component side)



PC 2(b) Cardiovascular System Card (back)



PC 3 (a) Peripheral Nervous System (component side)



PC 3(b) Peripheral Nervous System (back)

```
0000                TST:  ORG 0000H
0000    C30001            JMP STRT
003C                      ORG 003CH
003C    C32C01            JMP RS75
0100                      ORG 0100H
0100    3EC4        STRT: MVI A,0C4H   ;LOWER BYTE OF TIMER
0102    D30C              OUT 0CH
0104    3E49              MVI A,49H    ;HIGHER BYTE OF TIMER
0106    D30D              OUT 0DH
0108    21F008            LXI H,08F0H  ;SET SP
010B    F9                SPHL
010C    3ECF              MVI A,0CFH   ;SET CSR
010E    D308              OUT 08H
0110    3E1B              MVI A,1BH    ;SET INTR MASK
0112    30                DB 30H
0113    FB          WAIT: EI
0114    00          LOOP: NOP             ;LOOP
0115    C31401            JMP LOOP
0118                BCD:               ;BINARY TO BCD
                                       ;IN:A-BINARY
                                       ;OUT:A-BCD
                                       ;USES:B,C,D
0118    47                MOV B,A
0119    AF                XRA A
011A    0E08              MVI C,08H
011C    57          BCD1: MOV D,A
011D    78                MOV A,B
011E    17                RAL
011F    47                MOV B,A
0120    7A                MOV A,D
0121    D22501            JNC BCD2
0124    14                INR D
0125    82          BCD2: ADD D
0126    27                DAA
0127    0D                DCR C
0128    C21C01            JNZ BCD1
012B    C9                RET
012C    210008      RS75: LXI H,0800H
012F    DB00              IN 00H       ;READ ALL IN-PORTS
0131    77                MOV M,A
0132    23                INX H
0133    DB01              IN 01H
0135    77                MOV M,A
0136    23                INX H
0137    DB02              IN 02H
0139    77                MOV M,A
013A    23                INX H
013B    DB03              IN 03H
013D    77                MOV M,A
013E    23                INX H
013F    DB04              IN 04H
0141    77                MOV M,A
0142    23                INX H
0143    DB05              IN 05H
0145    77                MOV M,A
0146    23                INX H        ;WRITE OUTPUT PORTS
0147    7E                MOV A,M
0148    CD1801            CALL BCD
014B    D306              OUT 06H
014D    23                INX H
014E    7E                MOV A,M
014F    CD1801            CALL BCD
0152    D307              OUT 07H
0154    23                INX H
0155    7E                MOV A,M
0156    CD1801            CALL BCD
0159    D309              OUT 09H
015B    23                INX H
015C    7E                MOV A,M
015D    CD1801            CALL BCD
0160    D30A              OUT 0AH
0162    210008            LXI H,0800H
0165    7E                MOV A,M
0166    320608            STA 0806H    ;OUT1=IN1
```

```
0169    23               INX H
016A    7E               MOV A,M
016B    320708           STA 0807H    ;OUT2=IN2
016E    23               INX H
016F    7E               MOV A,M
0170    23               INX H
0171    BE               CMP M
0172    FA7601           JM PAS0
0175    7E               MOV A,M
0176    320808   PAS0:   STA 0808H    ;OUT3=MIN(IN3,IN4)
0179    23               INX H
017A    7E               MOV A,M
017B    23               INX H
017C    77               MOV M,A
017D    23               INX H
017E    BE               CMP M
017F    F28301           JP PAS1
0182    7E               MOV A,M
0183    320908   PAS1:   STA 0809H    ;OUT4=MAX(IN5,IN6)
0186    FB               EI
0187    C9               RET
                         END
NO PROGRAM ERRORS
```


SYMBOL TABLE

```
* 01

A      0007    B      0000    BCD    0118      BCD1   011C
BCD2   0125    C      0001    D      0002      E      0003
H      0004    L      0005    LOOP   0114      M      0006
PAS0   0176    PAS1   0183    PSW    0006      RS75   012C
SP     0006    STRT   0100    TST    0000 *    WAIT   0113
```

```
0000
0000    C30001      SIM    ;ORG 0000H
                            JMP STRT
003C                        ORG 003CH
003C    C33801              JMP RS75
0100                        ORG 0100H
0100    21F008      STRT:  LXI H,08F0H        ;SET SP
0103    F9                  SPHL
0104    AF          INIT :  XRA A              ;INITIALISATION
0105    210008              LXI H,0800H
0108    06E0                MVI B,0E0H
010A    77          INIT1:  MOV M,A
010B    23                  INX H
010C    05                  DCR B
010D    C20A01              JNZ INIT1
0110    3EC4        TIMR:  MVI A,0C4H         ;TIMER LOWER BYTE
0112    D30C                OUT 0CH
0114    3E49                MVI A,49H          ;TIMER HIGHER BYTE
0116    D30D                OUT 0DH
0118    3ECF                MVI A,0CFH         ;SET CSR
011A    D308                OUT 08H
011C    3E1B                MVI A,1BH
011E    30                  DB 30H             ;SET INTR MASK
011F    FB          WAIT:  EI
0120    00          LOOP:  NOP                ;LOOP
0121    C32001              JMP LOOP
0124                BCD:                    ;BINARY TO BCD
                                            ;IN:A-BINARY
                                            ;OUT:A-BCD
                                            ;USES:B,C,D
0124    47          BCDZ:   MOV B,A
0125    AF                  XRA A
0126    0E08                MVI C,08H
0128    57          BCD1:   MOV D,A
0129    78                  MOV A,B
012A    17                  RAL
012B    47                  MOV B,A
012C    7A                  MOV A,D
012D    D23101              JNC BCD2
0130    14                  INR D
0131    82          BCD2:   ADD D
0132    27                  DAA
0133    0D                  DCR C
0134    C22801              JNZ BCD1
0137    C9          BCDY:   RET
0138    210908      RS75:  LXI H,0809H
013B    7E                  MOV A,M            ;WRITE OUTPUT PORTS
013C    CD2401              CALL BCD
013F    D30A                OUT 0AH
0141    2B                  DCX H
0142    7E                  MOV A,M
0143    CD2401              CALL BCD
0146    D309                OUT 09H
0148    2B                  DCX H
0149    7E                  MOV A,M
014A    D307                OUT 07H
014C    2B                  DCX H
014D    7E                  MOV A,M
014E    D306                OUT 06
0150    2B                  DCX H              ;READ INPUT PORTS
0151    DB05                IN 05H
0153    86                  ADD M
0154    1F                  RAR
0155    77                  MOV M,A
0156    2B                  DCX H
0157    DB04                IN 04H
0159    86                  ADD M
015A    1F                  RAR
015B    77                  MOV M,A
015C    2B                  DCX H
015D    DB03                IN 03H
015F    86                  ADD M
0160    1F                  RAR
0161    77                  MOV M,A
0162    2B                  DCX H
```

```
0163   DB02               IN 02H
0165   86                 ADD M
0166   1F                 RAR
0167   77                 MOV M,A
0168   2B                 DCX H
0169   DB01               IN 01H
016B   86                 ADD M
016C   1F                 RAR
016D   77                 MOV M,A
016E   2B                 DCX H
016F   DB00               IN 00H
0171   86                 ADD M
0172   1F                 RAR
0173   77                 MOV M,A
0174            HEART:
0174   3A0408               LDA 0804H      ;CARDIAC CONTROL
0177   D619                 SUI 25         ;COMP OXY,REF
0179   FA8101               JM HEAR1       ;DIFF=OXY-REF
017C   3A0508               LDA 0805H
017F   D614                 SUI 20         ;IF OXY>REF COMP PRESS,REF
0181   00       HEAR1:      NOP            ;DIFF=PRESS-REF
0182   47                   MOV B,A        ;DIFF=2.DIFF
0183   C632                 ADI 50         ;SAVE DIFF
0185   320808               STA 0808H      ;INH=INHO+DIFF
0188   78                   MOV A,B
0189   2F                   CMA
018A   3C                   INR A
018B   C632                 ADI 50
018D   320908               STA 0809H      ;EXC=EXCO-DIFF
0190   161E     CNDRF:      MVI D,30      ;CONDITIONAL REFLEX
0192   1E7F                 MVI E,127     ;INPUT THRESHOLD
0194   2690                 MVI H,90H     ;ASSOCIATION THRESHOLD
0196   2E10                 MVI L,10H      ;HIGH OUTPUT
0198   3A0008   CR10 :      LDA 0800H      ;LOW OUTPUT
019B   BA                   CMP D
019C   FAC401               JM CR11
019F   3A0108               LDA 0801H
01A2   BA                   CMP D
01A3   FAB501               JM CR12
01A6   3A0A08               LDA 080AH
01A9   3C                   INR A
01AA   C2AF01               JNZ CR17
01AD   3EFF                 MVI A,255
01AF   320A08   CR17 :      STA 080AH
01B2   C3DF01               JMP CR13
01B5   3A0A08   CR12 :      LDA 080AH
01B8   D601                 SUI 1
01BA   D2BE01               JNC CR16
01BD   AF                   XRA A
01BE   320A08   CR16 :      STA 080AH
01C1   C3DF01               JMP CR13
01C4   3A0108   CR11 :      LDA 0801H
01C7   BA                   CMP D
01C8   FADB01               JM CR14
01CB   3A0A08               LDA 080AH
01CE   D601                 SUI 1
01D0   D2D401               JNC CR18
01D3   AF                   XRA A
01D4   320A08   CR18 :      STA 080AH
01D7   BB                   CMP E
01D8   F2DF01               JP CR13
01DB   7D       CR14 :      MOV A,L
01DC   C3E001               JMP CR15
01DF   7C       CR13 :      MOV A,H
01E0   320608   CR15 :      STA 0806H
01E3   3A0308   CR20 :      LDA 0803H
01E6   BA                   CMP D
01E7   FA1D02               JM CR21
01EA   3A0108               LDA 0801H
01ED   BA                   CMP D
01EE   FA0702               JM CR22
01F1   3A0208               LDA 0802H
01F4   BA                   CMP D
```

```
01F5  FA3F02          JM CR23
01F8  3A0B08          LDA 080BH
01FB  3C              INR A
01FC  C20102          JNZ CR27
01FF  3EFF            MVI A,255
0201  320B08   CR27 : STA 080BH
0204  C33F02          JMP CR23
0207  3A0208   CR22 : LDA 0802H
020A  BA              CMP D
020B  F23F02          JP CR23
020E  3A0B08          LDA 080BH
0211  D601            SUI 1
0213  D21702          JNC CR26
0216  AF              XRA A
0217  320B08   CR26 : STA 080BH
021A  C33F02          JMP CR23
021D  3A0108   CR21 : LDA 0801H
0220  BA              CMP D
0221  FA3B02          JM CR24
0224  3A0208          LDA 0802H
0227  BA              CMP D
0228  FA3B02          JM CR24
022B  3A0B08          LDA 080BH
022E  D601            SUI 1
0230  D23402          JNC CR28
0233  AF              XRA A
0234  320B08   CR28 : STA 080BH
0237  BB              CMP E
0238  F23F02          JP CR23
023B  7D       CR24 : MOV A,L
023C  C34002          JMP CR25
023F  7C       CR23 : MOV A,H
0240  320708   CR25 : STA 0807H
0243  FB              EI
0244  C9              RET
                      END
NO PROGRAM ERRORS
```


SYMBOL TABLE

```
* 01

A      0007      B      0000      BCD    0124      BCD1   0128
BCD2   0131      BCDY   0137 *    BCDZ   0124 *    C      0001
CNDRF  0190 *    CR10   0198 *    CR11   01C4      CR12   01B5
CR13   01DF      CR14   01DB      CR15   01E0      CR16   01BE
CR17   01AF      CR18   01D4      CR20   01E3 *    CR21   021D
CR22   0207      CR23   023F      CR24   023B      CR25   0240
CR26   0217      CR27   0201      CR28   0234      D      0002
E      0003      H      0004      HEAR1  0181      HEART  0174 *
INIT   0104 *    INIT1  010A      L      0005      LOOP   0120
M      0006      PSW    0006      RS75   0138      SIM    0000 *
SP     0006      STRT   0100      TIMR   0110 *    WAIT   011F *
```